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Clinical Profile of Elderly Patients on Anticoagulation Therapy with Warfarin

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Abstract

Aim: The National Geriatrics and Gerontology Hospital (HNGG) handles tens of patients which receive oral anticoagulation therapy and which come from different provinces of the country; the study did a clinical and socio-demographic characterization of the anticoagulated elderly population that receives control and treatment in the outpatient consultation clinic for anticoagulation patients during the period 2006-2007.

Methods: 141 elderly patients that received anticoagulation therapy with warfarin during the period 2006-2007 were studied. A descriptive analysis of the demographic and clinical characteristics of all the patients was performed, emphasizing on the causes of anticoagulation, comorbidities, number of drugs used; cognitive, functional and social status, quality of the anticoagulation, reasons for suspension of the treatment and complications.

Results: The average age of the patients was of 78 years. Most of the population comes from the Central, Desamparados and Escazú cantons of the Province of San Jose and have a low academic level, which does not surpass primary schooling. Atrial fibrillation was the main diagnostic, which justified the anticoagulation therapy. The most important comorbidity was the combination between heart failure and hypertension. Most of the population uses 5 or more drugs apart from warfarin. The majority of the individuals in the group studied showed an adequate cognitive status, total functional independence or a minimum dependency, and they did not show a social risk. There was a high variability in the therapeutical effects of warfarin, which was reflected in the difficulty to reach optimal levels of INR in a large part of the control consultations and in the amount of treatment adjustments necessary to improve its quality. The main reasons to suspend the anticoagulation therapy were bad adherence to treatment, a poorly committed social network and the adverse effects related to over anticoagulation (minor bleedings). There was a similar incidence of minor and major bleedings (4.3%), and a mortality of 1.4%.

Conclusion: The handling of elderly patients that receive oral anticoagulation therapy is highly comple, an aspect that is reflected both in its demographic as well as clinic profile. The complications associated to the therapy, did not differ from the ones reported at an international level.

Key words: anticoagulation, warfarin, bleeding, thrombosis.

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Abreviaturas: ACO: Anticoagulación oral; BARTHEL, Test de valoración funcional de actividades básicas de vida diaria. HNGG, Hospital Nacional de Geriatría y Gerontología; Mg, Miligramos; INR, Índice Normalizado Internacional; MMSE, Mini Mental State Examination - Test de tamizaje para Deterioro Cognitivo.
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Aging is considered a major cardiovascular risk factor. Heart diseases are the most common cause of death among the elderly.[1] Due to increased longevity and declining fertility, the geriatric population has considerably increased in industrialized countries. By 2020, the population age 80 years and above is expected to rise from 3.7% to 7.5%. [2]

Anticoagulation therapy is one of the main treatments in elderly patients with heart disease. The benefits of this therapy in said population are well established, however, it is the most vulnerable group to adverse effects. This could be further exacerbated by the presence of diseases at high risk for thromboembolism potential, such as atrial fibrillation.[3-6]

Several factors inherent to the elderly population add complexity to anticoagulation therapy. Among these factors, the following stand out: age-dependent alterations of homeostasis, characterized by increased platelet activity, [7,8] blood stasis, and vessel wall degeneration with endothelial dysfunction.[9] The pharmacokinetic and pharmacodynamic aspects related to the absorption, distribution, metabolism and clearance of antithrombotic drugs must be considered when commencing anticoagulation therapy. Polypharmacy, a common phenomenon in the geriatric population, generates a greater risk of adverse drug-drug interactions.[10]

Currently, there is no general consensus about the definition of elderly; therefore, to generalize the findings of different studies is problematic. The elderly population is frequently excluded from cardiovascular clinical trials, therefore current treatments have been developed on the basis of younger populations. This is one of the reasons for the underutilization of anticoagulation therapy in elderly patients.[11-13]

In general, treatment with oral anticoagulants is associated with a 0.3% to 0.5% of major bleeding per year.[14] There is a tendency towards a 2- to 3-fold increase in minor bleeding and intracranial haemorrhages among elderly patients.[14, 15] This is another important reason that explains physicians' tendency to underutilize this treatment due to the high risk of bleeding and falls, which can cause serious hemorrhagic complications.[16] The doses required to maintain adequate INR ranges in patients over 60 years of age decreases with increasing age, possibly due to the reduction in the clearance of these drugs with ageing. Therefore, it should be taken into consideration whenever anticoagulation therapy commences.[17, 18]

The *Hospital Nacional de Geriatría and Gerontología* [National Geriatrics and Gerontology Hospital] provides medical care to a significant number of patients that receive oral anticoagulation therapy and who come from different provinces in the country. In this study, the general information of a group of patients that received anticoagulation therapy with warfarin at the HNGG was analysed, in order to determine the clinical and sociodemographic profile of this population.

Materials and methods

An observational- descriptive study was carried out about the total number of patients that received anticoagulation therapy with warfarin, who attended outpatient control consultation at the HNGG, from January 1, 2006 to December 31, 2007. The analysis performed was retrospective, using the information in each patient's medical records. Research was approved by the *Comité de Ética en Investigación del Hospital Nacional de Geriatría y Gerontología* [HNGG Research Ethics Committee] and it did not require informed consent because it was a non-interventional study that safeguarded the confidentiality of the subjects included.

A sample was obtained of 141 patients that received anticoagulation therapy with warfarin between January 1, 2006 and December 31, 2007 and who received periodical outpatient consultation attention at the HNGG. The following variables were determined: age, sex, origin, education level, reason for anticoagulation, comorbidities, polypharmacy (use of 5 or more drugs), cognitive status (for its assessment, the Mini Mental State Examination for cognitive impairment detection- MMSE- was used), [19] functional status (for its assessment, the Basic Activities of Daily Living Index – BARTHEL- was used), [20] social risk (the factors considered were: poor adherence to treatment, low commitment of family network with the patient's monitoring and institutionalization), number of control appointments,

average number of treatment adjustments (number of adjustments in the warfarin dose, either increase or decrease as a result of control appointments), quality of the anticoagulation therapy (assessed according to International Normalised Ratio- INR- levels: optimal 2-3, sub therapeutic <2 and supra therapeutic >3), warfarin dose used, reasons for suspension of treatment (medical, psychological, functional and social), and complications.

The inclusion criteria comprised the patients that received anticoagulation therapy with warfarin, under control and monitored at the HNGG outpatient consultation between January 1, 2006 and December 31, 2007. The exclusion criteria used were: patients treated with other therapies different from warfarin and incomplete information in the medical records.

Absolute and relative frequency distributions were calculated for all variables; for quantitative variables, the mean, median and standard deviation values were found.

To determine the number of patients that achieved adequate levels of anticoagulation, the "acceptable level of normality" was defined by obtaining optimal levels of INR (2-3) in at least 50% of the appointments attended during the analyzed period.

Comparisons according to age and sex of patients were made for diagnostic variables, type of complication, polypharmacy, comorbidities, warfarin dose used, cognitive ability, functional ability and social risk. The results obtained from the comparison of these variables were tested for statistical significance.

For qualitative variables, chi-square was applied; for the quantitative ones, the student t test or variance analysis was used, depending on the number of groups to be compared. When the variance analysis was found to be statistically significant, the Bonferroni and Tukey post-tests were performed to identify the groups that showed differences.

A Pearson correlation was performed using the quantitative variables number of consultations and treatment adjustments. The information was summarized in tables and graphs. In both analyses, significance is considered at a confidence level of <0.05. The information was transferred to a database and processed using the SPSS statistical programme version 13 and Excel, in order to make charts.

Results

The study's overall population (N=141) had a similar distribution per sex, an average age of 78.3 years, standard deviation (SD) of 7.4 years, median, 78 years.

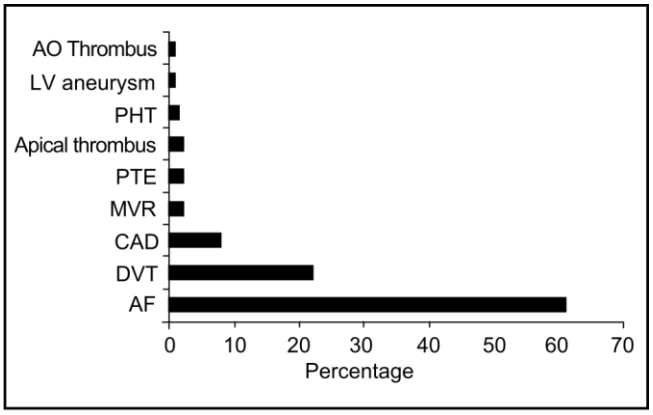

Figure 1 Distribution of the main diagnoses to prescribe oral anticoagulation with warfarin, HNGG. Period 2006-2007

AO= aortic, LV= left ventricle, PHT= pulmonary hypertension, PTE= Pulmonary thromboembolism, MVR= mitral valve replacement, CAD= coronary artery disease, DVT= deep vein thrombosis, AF= atrial fibrillation

A majority of the patients came from the province of San José (Central Canton 34.2%, Desamparados 22.2% and Escazú10.3%) and 74.5% had a low academic level that did not exceed primary school education.

Atrial fibrillation was the main diagnosis for prescription of anticoagulation therapy 61% (Figure 1). The combination of heart failure and hypertension were the most prevalent comorbidities, 37.6%.

Apart from warfarin, the majority of the population used 5 or more drugs 80.9% (Table 1).

The analyzed cases showed an adequate cognitive capacity 72.3%, total functional independence or minimum functional dependence 85.8% and did not show social risk factors 85.1%.

It was determined that 42.6% of patients had acceptable levels of INR, no statistically significant

differences between men and women were found, p=0.78 (Table 2). In the group of patients who showed an unacceptable quality of anticoagulation, INR ranges varied from under-anticoagulation to over-anticoagulation in a same case, thus, the subdivision of the latter group could not be established.

The average warfarin dose used by patients who achieved optimal INR levels in most of their consultation visits was 3.7 mg per day; while in the group that did not reach optimal levels of anticoagulation the average dose was 3.5 mg per day, no statistically significant difference was found (p=0.55).

There was a high variability in the therapeutic effect of warfarin. This was reflected in the difficulty to achieve optimal levels of INR in most of the control appointments and in the number of necessary adjustments to the amount of treatment required to optimize it (r2=0.89, p=0.00).

Table 1. Number of drugs used by the population studied, excluding warfarin, according to sex, HNGG. Period 2006-2007

	Male		Female		Total	
Polypharmacy	N°	%	N°	%	N°	%
1	2	3.2	0	0.0	2	1.4
2	1	1.6	1	1.3	2	1.4
3	3	4.8	3	3.8	6	4.3
4	9	14.3	8	10.3	17	12.1
5 to 12	48	76.2	66	84.6	114	80.9
Total	63	100.0	78	100.0	141	100.0

Table 2. Quality of anticoagulation in the population studied, according to sex, HNGG. Period 2006-2007

Quality of anticoagulation	Male		Female		Total	
	N°	%	N°	%	N°	%
Acceptable	26	41.3	34	43.6	60	42.6
Unacceptable	37	58.7	44	56.4	81	57.4
Total	63	100.0	78	100.0	141	100.0

The main reasons to suspend anticoagulation therapy were bad adherence to treatment, poor family supervision in the patient's monitoring and adverse effects associated to anticoagulation, such as minor bleeding.

There was a similar incidence of minor and major bleeding 4.3%, the latter were distributed in central nervous system bleeding and retroperitoneal haematomas. The mortality rate was 1.4% and no thrombotic events associated with subtherapeutic levels of anticoagulation were registered nor cases of skin necrosis secondary to the use of warfarin (Table 3).

Table 3. Distribution of minor and major bleedings in the population studied, according to sex, HNGG. Period 2006-2007

Type of complication	Sex		Total
	Masculino	Femenino	
Haemorrhagic CVA	1	1*	2
Epistaxis	1	0	1
Ecchymosis	1	2	3
Gingivorrhagia	1	0	1
Retroperitoneal hematoma	0	2	2
Hematuria	1	2	3
Petechiae	0	1	1
Allergic reaction	1	0	1
Gastrointestinal haemorrage	0	1*	1
Total	6	9	15

* Died

CVA= cerebrovascular acccident

Discussion

The clinical profile analyzed in this study, of elderly patients who received oral anticoagulation therapy with warfarin, is highly complex. This is reflected in both, their sociodemographic and clinical characteristics.

With aging, the risk of suffering from diseases with high potential for thromboembolism increases significantly. Atrial fibrillation is one of the pathologies that evidences this fact. This disorder in cardiac rhythm increases as the population ages and its association with cerebral embolism is enhanced; as demonstrated by Framingham's study, where the population showed 5.6 times greater risk of developing this asociación.[3, 4] As shown in this study, the main cause of anticoagulation was atrial fibrillation; all of which is consistent with the literature.

Several factors inherent to the elderly population make anticoagulant therapy a complex one. Among them, biological and pharmacological factors stand out, as they challenge the attainment of adequate levels of anticoagulation and can generate adverse effects due to undesirable interactions.[7] Elderly patients who received anticoagulation therapy in this study showed two particular characteristics: the presence of multiple comorbidities, mainly of a cardiovascular type, and polypharmacy. It is important to pay close attention to these factors when commencing oral anticoagulation therapy with warfarin in elderly patients, in order to endeavour to reduce the complications associated to treatment, as aging by itself entails an increase in platelet activity, blood stasis and vessel wall degeneration with of endothelial dysfunction.[8, 9]

The comprehensive assessment of elderly patients includes the assessment of 4 key areas: medical, psychological, functional and social. There is scant evidence on the role of mental, functional and social integrity on the elderly patient with regard to anticoagulation therapy, however existing studies have shown a higher rate of complications in those patients with impaired cognitive ability, significant functional limitations and at social risk.[22, 23] It was possible to establish for most of the patients studied, in an objective manner (through validated instruments), an appropriate cognitive ability, functional status and social environment. In terms of risk-benefit analysis, it is important to consider these factors in an integral manner when selecting a patient as a candidate for oral anticoagulation therapy. A assessment of the four functions (medical, psychological, functional and social) is an important tool to decide whether the patient is suitable for chronic anticoagulant treatment or for a more conservative management.[21]

With regard to the quality of anticoagulation, the results show that optimal INR levels were not obtained from the majority of the patients studied, a phenomenon that has a multi-factor basis. This was demonstrated by analyzing the warfarin's therapeutic response in both, patients who reached optimal levels of INR and in those who did not reach them. Although both groups used similar drug doses (mg), the therapeutic response was different from one patient to another. This individual variability justified a greater amount of control appointments in different patients due to dose adjustments prescribed to try to optimize anticoagulation.

An important aspect of the study is that there were cases in which assessment of the treatment's risk-benefit led to the decision to suspend anticoagulation therapy. The most important reasons for the suspension of therapy in the study group were of a social and medical character. It is noteworthy that, although the percentage of treatment suspension was low, lack of family monitoring in relation to medication adherence was the most important factor influencing the suspension of medication. This occurs because warfarin has a low safety profile and is a drug that should be monitored periodically; therefore the elderly patient requires support and supervision in order to obtain optimal results in its therapy and to prevent associated complications.[24,25] Therefore, assessment of the social environment is a prerequisite prior to commencing chronic warfarin therapy in the elderly.

The risk of complications associated with OAC therapy significantly rises with increasing age, however if this therapy is practised in a comprehensive manner, the complications do not differ significantly when compared with other age groups and the benefit in terms of secondary prevention is greater than that obtained in younger populations. The behaviour of complications in this study for both, major and minor bleeding events, was similar to that described by the literature,[14,15] and mortality associated to this therapy was very close to that established in different reports.[16]

Within the study's limitations, it is worth mentioning its type of design. Since this is a descriptive study, based on data collection from medical records in the anticoagulation outpatient consultation, important information about the therapy from the emergency and hospitalization services' notes could have been omitted. Regarding the statistical analysis of the variables, the quality of anticoagulation was difficult to obtain; because of the multi-factor variability response to treatment, most patients showed at some point during their monitoring appointments optimal levels of anticoagulation, under-coagulation and over-coagulation. For this reason, patients were grouped into those who had acceptable and unacceptable levels as a result of the author's personal criteria, as this classification is not supported by international literature.

Given the complexity of administering oral anticoagulation therapy to elderly patients, it is necessary to implement an interdisciplinary management approach, which should include the establishment of anticoagulation clinics that promote the participation of different health specialists, conduct a close monitoring of the patient and that involve in its management both, the patient and its family.

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Abbreviations: ACO: oral anticoagulation; BARTHEL, Barthel's Index of Activities of Daily Living. HNGG, Hospital Nacional de Geriatría y Gerontología; Mg, milligrams; INR, International Normalized Ratio; MMSE, Mini Mental State Examination.
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