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Original article

Anticoagulation Control in Patients With Nonvalvular Atrial Fibrillation Attended at Primary Care Centers in Spain: The PAULA Study

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ABSTRACT

Introduction and objectives: To determine the current status of anticoagulation control in patients with nonvalvular atrial fibrillation treated with vitamin K antagonists in the primary care setting in Spain.
Methods: The PAULA study was a multicenter cross-sectional/retrospective observational study conducted throughout Spain. The study included patients with nonvalvular atrial fibrillation who had been receiving vitamin K antagonist therapy during the past year and were attended at primary care centers. International normalized ratio (INR) values over the past 12 months were recorded. The degree of anticoagulation control was defined as the time the patient had remained within the therapeutic range and was determined by both the direct method (poor control < 60%) and by the Rosendaal method (poor control < 65%).
Results: The study assessed 1524 patients (mean age, 77.4 ± 8.7 years; 48.6% women; 64.2% in permanent atrial fibrillation; $CHADS_2$ mean, 2.3 ± 1.2; CHA_2DS_2-VASc, 3.9 ± 1.5, and HAS-BLED, 1.6 ± 0.9). The mean number of INR readings recorded per patient was 14.4 ± 3.8. A total of 56.9% of patients had adequate INR control according to the direct method and 60.6% according to the Rosendaal method. The multivariate analysis identified the following predictors for poor INR control: female sex, dietary habits potentially affecting anticoagulation with vitamin K antagonists, multidrug therapy, and a history of labile INR.
Conclusions: Approximately 40% of patients (43.1% by the direct method and 39.4% by the Rosendaal method) with nonvalvular atrial fibrillation who were receiving anticoagulation therapy with vitamin K antagonists in primary care in Spain had poor anticoagulation control during the previous 12 months.

Control de la anticoagulación en pacientes con fibrilación auricular no valvular asistidos en atención primaria en España. Estudio PAULA

Palabras clave:
Fibrilación auricular no valvular
Antagonistas de la vitamina K
Control de la razón internacional normalizada
Rosendaal

RESUMEN

Introducción y objetivos: Conocer la situación actual del control de la anticoagulación en pacientes con fibrilación auricular no valvular tratados con antagonistas de la vitamina K en atención primaria en España.
Métodos: PAULA es un estudio observacional transversal/retrospectivo y multicéntrico de ámbito nacional. Se incluyó a pacientes con fibrilación auricular no valvular en tratamiento con antagonistas de la vitamina K durante el último año atendidos en las consultas de atención primaria. Se registraron los valores de la razón internacional normalizada (INR) durante los últimos 12 meses. El grado de control de la anticoagulación se determinó mediante el tiempo en rango terapéutico, tanto por el método directo (mal control < 60%) como por el método de Rosendaal (mal control < 65%).

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Resultados: Se evaluó a 1.524 pacientes (media de edad, 77,4 ± 8,7 años; el 48,6% mujeres; el 64,2% en fibrilación auricular permanente; media de $CHADS_2$, 2,3 ± 1,2; de CHA_2DS_2-VASc, 3,9 ± 1,5, y de HAS-BLED, 1,6 ± 0,9). El número medio de determinaciones de la INR registradas por paciente fue 14,4±3,8. El 56,9% de los pacientes tenían un adecuado control por la INR según el método directo y el 60,6% según el método de Rosendaal. En el análisis multivariable, fueron predictores de mal control de la INR el sexo femenino, los hábitos dietéticos que pudieran afectar a la anticoagulación con antagonistas de la vitamina K, la polimedicación y los antecedentes de razón INR lábil.

Conclusiones: Aproximadamente el 40% de los pacientes (el 43,1% por el método directo y el 39,4% por el método de Rosendaal) con fibrilación auricular no valvular anticoagulados con antagonistas de la vitamina K en atención primaria en España presentan un control de la anticoagulación inadecuado durante los 12 meses previos.

Abbreviations

AF: atrial fibrillation
INR: international normalized ratio
NVAF: nonvalvular atrial fibrillation
VKAs: vitamin K antagonists

INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia in the general population, with an estimated prevalence of about 2%, a figure that rises with age and comorbidities.[1] Several studies have recently been conducted in Spain to understand the situation of AF in clinical practice. The VAL-FAAP study[2] analyzed nearly 120 000 patients attended at primary care centers and observed that 6.1% of patients had AF. In the general population older than 40 years, the prevalence of AF in Spain was 4.4%.[3] Among patients with hypertension and older than age 65 years in the Valencian Community, 10.3% had AF.[4]

Compared with patients without AF, patients with AF have a 2-fold risk of death and up to 5-fold risk of stroke.[5] Atrial fibrillation-related stroke has a higher mortality and a higher risk of recurrences and tends to result in more sequelae.[6] In most patients with AF, long-term oral anticoagulation is indicated to prevent thromboembolic complications.[2] For this purpose, vitamin K antagonists (VKAs) have been widely used for decades because they can reduce the risk of stroke by about 64%.[7]

However, VKAs have important limitations that usually condition their use in clinical practice for nonvalvular AF (NVAF).[2,8] These include narrow therapeutic window, drug and food interactions, and variable metabolism, which require regular follow-up of anticoagulation status and frequent dose titration.[9,10] It is crucial that the international normalized ratio (INR) of patients receiving VKA therapy be within therapeutic range to reduce the risk of thromboembolic and hemorrhagic complications. In fact, time to onset of stroke has been shown to significantly improve in warfarin-treated patients with NVAF and $CHADS_2$ score ≥ 2 compared with untreated patients, but only in treated patients who were within therapeutic range $> 70\%$ of the time.[11]

Therefore, to manage this population adequately, it is essential to identify the degree of INR control among patients with NVAF who are receiving VKA anticoagulation therapy. Several studies[12,13] have investigated the degree of INR control in a specific geographic area of Spain or using only a small number of INR values. However, the PAULA study (*Perspectiva Actual de la sitUación de la anticoaguLación en la práctica cínica de Atención primaria* [Current perspective of anticoagulation in clinical practice in the primary care setting]) was conducted to understand the situation of anticoagulation control over a long period among patients with NVAF who are receiving VKAs in primary care clinical practice throughout Spain. This study specifically looked at anticoagulation in the clinical practice setting at primary care centers.

METHODS

The PAULA study was based on an observational cross-sectional/retrospective, multicenter, national design, and its main aim was to identify anticoagulation control of patients with NVAF who were receiving anticoagulation VKA therapy at primary care centers in Spain last year. The study had the scientific backing of three Spanish primary care societies (SEMERGEN, semFYC, and SEMG).

To perform the study, a scientific committee was formed with 2 cardiologists, 1 biostatistician, and 3 general practitioners who were experts in cardiovascular disease and represented the 3 Spanish primary care societies. The general practitioners chose 9 regional coordinators (Appendix 1 of the supplementary material), who in turn selected 139 investigators (Appendix 2 of the supplementary material) from 99 health centers located throughout the different autonomous communities (except for La Rioja, for logistical reasons) according to the proportion of regional inhabitants, thus ensuring numbers of patients representative of the national territory (Table 1). The regional coordinator initially selected the investigators based on their clinical and research skills, and the choice was then approved by the scientific committee. Each investigator had to include at least the first 10 consecutive patients who met all inclusion criteria and none of the exclusion criteria, who came for routine anticoagulation follow-up, and who gave consent to participate in the study. All patients were recruited between February and June 2014.

The inclusion criteria were as follows: *a)* patients of either sex and 18 years of age or older; *b)* patients with NVAF who had been receiving VKA therapy for at least the past year at a primary health care center under routine clinical practice conditions; *c)* patients for whom at least 80% of INR controls were available from the past year, and *d)* patients who had given written informed consent to participate in the study after they had read and understood the patient information sheet. Patients were excluded if they had cognitive impairment that prevented them from correctly understanding the patient information sheet or informed consent or if they had participated in any clinical trial in the past 12 months.

The study comprised a single visit, that coincided with one of the patient's regular follow-up visits. The data were collected from