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Original article

Adherence to recommendations of the Therapeutic Positioning Report about treatment with oral anticoagulants in elderly patients with atrial fibrillation. The ESPARTA study☆

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ABSTRACT

Background and objective: To evaluate the adherence to the recommendations in clinical practice performed by the Therapeutic Positioning Report (TPR) of the Spanish Agency of Medicines and Sanitary Products about the treatment with oral anticoagulants in patients aged ≥75 years old with nonvalvular atrial fibrillation (NVAF) treated in Internal Medicine departments in Spain.

Patients and methods: Observational, cross-sectional and multicenter study in which 837 patients aged ≥75 years old with NVAF, with stable treatment with oral anticoagulants at least 3 months before inclusion, and that had started treatment with oral anticoagulants before the inclusion period were included.

Results: Mean age was 83.0 ± 5.0 years old, mean $CHADS_2$ score 3.2 ± 1.2, mean CHA_2DS_2-VASc score 5.0 ± 1.4, and mean HAS-BLED score 2.1 ± 0.9. A percentage of 70.8 of patients were treated with vitamin K antagonists (VKA) and the rest of patients with direct oral anticoagulants (DOACs). A percentage of 65.6 of patients treated with VKA did not follow the recommendations made by the TPR compared with 43.0% of patients treated with DOACs ($p < 0.0001$). In the case of VKA, the main reason for being considered as not appropriate according to the TPR was having poor control of anticoagulation and not switching to DOACs, whereas in the case of DOACs, it was not receiving the adequate dose according to the TPR.

Conclusions: In a high proportion of anticoagulated elderly patients with NVAF in Spain, the recommendations performed by the TPR are not followed, particularly with VKA, since patients are not switched to DOACs despite time in therapeutic range.

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Seguimiento de las recomendaciones del Informe de Posicionamiento Terapéutico sobre el tratamiento con anticoagulantes orales en pacientes ancianos con fibrilación auricular. Estudio ESPARTA

Palabras clave:
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R E S U M E N

Fundamento y objetivo: Evaluar en la práctica clínica el cumplimiento de las recomendaciones del Informe de Posicionamiento Terapéutico (IPT) de la Agencia Española de Medicamentos y Productos Sanitarios sobre el tratamiento con anticoagulantes orales en pacientes ≥75 años con fibrilación auricular no valvular (FANV) atendidos en unidades de Medicina Interna en España.
Pacientes y métodos: Estudio observacional, transversal y multicéntrico, en el que se incluyeron 837 pacientes ≥75 años con FANV en tratamiento estable con anticoagulantes orales durante los 3 meses previos a la inclusión y que hubiesen iniciado dicho tratamiento antes de comenzar el período de inclusión.
Resultados: La edad media fue de 83,0 ± 5,0 años, el $CHADS_2$ medio 3,2 ± 1,2, el CHA_2DS_2-VASc 5,0 ± 1,4 y el HAS-BLED 2,1 ± 0,9. El 70,8% de los pacientes estaba en tratamiento con antagonistas de la vitamina K (AVK) y el resto con anticoagulantes orales de acción directa (ACOD). El 65,6% de los pacientes con AVK no siguieron las recomendaciones del IPT frente al 43,0% de los pacientes con ACOD (p < 0,0001). En el caso de los pacientes con AVK, el motivo principal para ser considerado como no adecuado fue presentar un mal control de la anticoagulación y no cambiar a un ACOD, mientras que en el caso de los ACOD fue recibir una dosis inadecuada según el IPT.
Conclusiones: En un porcentaje elevado de pacientes ancianos con FANV anticoagulados en España no se siguen las recomendaciones realizadas por el IPT, especialmente con los AVK, al no realizarse el cambio a ACOD a pesar de un tiempo en rango terapéutico inadecuado.

Introduction

The prevalence of atrial fibrillation (AF) increases significantly with age, exceeding 10% after the age of 70, rising to 18% from the age of 80.[1]

Elderly patients with AF is a complex patient due to the high number of associated comorbidities, cognitive deterioration, the risk of falling or frequent polypharmacy, among others, which greatly interfere with treatment.[2–5] All this means that the risk of death and complications is increased in this population.[6]

Although AF increases the global risk of stroke, it increases with age, especially after the age of 75.[7] Stroke associated with AF has a high morbidity and mortality, which is more striking in the elderly population.[8] Even though, unless contraindicated, all patients ≥75 years of age with AF should receive oral anticoagulation,[9] the reality is that the use of anticoagulant treatment decreases with increasing age and this has been associated with an increased risk of stroke and death.[10,11]

Globally, compared to warfarin, direct oral anticoagulants (DOAC) have been associated with significant reductions in the risk of stroke, particularly intracranial bleeding and mortality, without increasing the risk of major bleeding.[12] It seems that these results are also consistent in the elderly population.[13,14] In addition, DOAC overcome many of the limitations of vitamin K antagonists (VKA), which could facilitate the increased use of anticoagulation in this population.[15]

However, information from clinical trials is not always transferable to the "real life" patient, and although clinical practice studies have been published in recent years, information is still scarce in the elderly population.[16] On the other hand, the Spanish Agency for Medicines and Medical Devices published a Therapeutic Positioning Report (TPR) on the use of oral anticoagulants in patients with non-valvular AF (NVAF), making a series of recommendations about which situations would call for an anticoagulation indication, also, which cases would be compatible with maintaining the treatment with VKA and which cases would be compatible with the use of DOAC.[17]

Unfortunately, information about the treatment of anticoagulation in elderly patients with NVAF in Spain is very scarce, and it is not known if the recommendations made about anticoagulation in this population are followed correctly under routine clinical practice. ESPARTA was an observational, cross-sectional and multicenter study, whose main objective was to evaluate, in routine clinical practice, compliance with TPR recommendations on oral anticoagulant treatment in patients with AF ≥75 years of age in Internal Medicine units in Spain.

Material and methods

Patients ≥75 years of age of both sexes, with a diagnosis of NVAF, who were being treated by Internal Medicine units (outpatient or hospitalized) in Spain, under stable treatment with oral anticoagulants during the 3 months prior to inclusion in the study (excluding the period of adjustment of the initial dose in the case of VKA) and who had granted written informed consent were included in the ESPARTA study. Patients with mitral stenosis or other significant valve disease requiring specific or scheduled treatment (prosthesis, valvuloplasty), patients who had participated in clinical trials with DOAC in the 6 months prior to the inclusion in the study, as well as patients with any type of disorder that alters the ability to understand or complete the questionnaires were excluded. The study was approved by the reference Clinical Research Ethics Committee (La Princesa University Hospital of Madrid) and by the local clinical research ethics committees of the different participating centres that required it.

The study was carried out in Internal Medicine units distributed nationwide, according to routine clinical practice. A total of 63 centres participated in the study. The inclusion period lasted 5 months, starting in October 2015. The study consisted of a single visit, which coincided with the time of patient inclusion in the study, which was carried out consecutively and according to scheduled routine clinical practice visits. Sociodemographic and clinical data, including the presence of cardiovascular risk factors and the history of cardiovascular diseases, were collected by each investigator from the patient's medical records and were collected through an electronic Case Report Form by means of a web page created for that purpose.

The thromboembolic risk was stratified using the $CHADS_2$ and CHA_2DS_2-VASc scores and the risk of bleeding using the HAS-BLED score.[18,19] The anticoagulant treatment was analyzed (type, duration, previous antithrombotic treatment, time in therapeutic range