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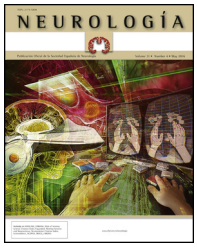

ORIGINAL ARTICLE

Ischaemic stroke in patients treated with oral anticoagulants☆,☆☆

L.M. Cano*, **P. Cardona**, **H. Quesada**, **B. Lara**, **F. Rubio**

Servicio de Neurología, Hospital Universitari de Bellvitge, IDIBELL, L'Hospitalet de Llobregat, Barcelona, Spain

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KEYWORDS
Oral anticoagulants;
Ischaemic stroke;
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Abstract
Introduction: Cardioembolic stroke is associated with poorer outcomes. Prevention is based on oral anticoagulant (OAC) therapy. Haemorrhage is the main complication of OACs, which are sometimes ineffective.
Patients and methods: We retrospectively reviewed 1014 consecutive patients who suffered an ischaemic stroke between 2011 and 2013, analysing those who were receiving OAC treatment at stroke onset (107 patients in total) with special attention to aetiology, outcomes, and INR value in the acute phase.
Results: The mean age (SD) was 71.9 (10) years. Patients had been treated with OACs for 5.9 (5.5) years; 98.1% of them were being treated for heart disease. INR was <2 in 77 patients (72%), and 30 patients (28%) had an INR ≥ 2. Nine patients (8.4%) had INR values within the therapeutic range. According to TOAST classification criteria, 88.8% of strokes were cardioembolic and 1.9% were atherothrombotic.

Anticoagulation therapy was discontinued in 48 patients (44.9%) due to haemorrhagic transformation (24 patients), extensive infarction (23), or endarterectomy (1). Therapy was resumed in 24 patients (50%) after a mean lapse of 36 days. This was not possible in the remaining patients because of death or severe sequelae.

New OACs (NOACs) were prescribed to 9 patients (18.7% of all potential candidates). At 3 months, patients with INR > 1.7 in the acute phase exhibited better outcomes than patients with INR ≤ 1.7 (mRS 0-2 in 62% vs 30.8%; death in 10% vs 38.4%; $P = .0004$).
Conclusions: Some patients taking OACs suffer ischaemic strokes that are usually cardioembolic, especially if INR is below the therapeutic range. OACs can be resumed without complications, and NOACs are still underused. Despite cases in which treatment is ineffective, outcomes are better when INR is above 1.7 at stroke onset.

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* Corresponding author.
E-mail address: lcano@bellvitgehospital.cat (L.M. Cano).

PALABRAS CLAVE
Anticoagulantes orales;
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Ictus isquémico en pacientes en tratamiento anticoagulante por vía oral

Resumen
Introducción: Los ictus cardioembólicos tienen peor pronóstico. Su prevención se basa en el tratamiento anticoagulante por vía oral (ACO), cuya principal complicación es el sangrado y, en ocasiones, su ineficacia.
Pacientes y métodos: Se ha revisado retrospectivamente a 1.014 pacientes consecutivos que presentaron ictus isquémico entre 2011 y 2013. De ellos, hemos analizado a los 107 pacientes en tratamiento con ACO en el momento del ictus, con especial atención a su etiología, evolución y valour del INR en la fase aguda.
Resultados: La edad media ± desviación estándar fue de 71,9 ± 10 años. Tomaba ACO desde hacía 5,9 ± 5,5 años el 98,1% por cardiopatía. Setenta y siete pacientes (72%) tenían INR < 2 y 30 (28%) un INR ≥ 2. Se encontraban en rango terapéutico 9 pacientes (8,4%). La etiología según TOAST fue cardioembólica en el 88,8% y aterotrombótica en el 1,9%.

Se suspendió la anticoagulación en 48 pacientes (44,9%): 24 por transformación hemorrágica, 23 por infarto extenso y uno por endarterectomía. Se reintrodujo en 24 de ellos (50%), a los 36 días de media; en los restantes, no fue posible por fallecimiento o secuelas severas.

En 9 pacientes (18,7% de potenciales candidatos) se iniciaron nuevos ACO (NACO). La evolución a los 3 meses fue mejor si el INR en la fase aguda > 1,7 respecto al INR ≤ 1,7 (mRS 0-2: 62% vs. 30,8% y fallecimiento 10% vs. 38.4%; p = 0,0004).
Conclusiones: Algunos pacientes con ACO presentan ictus isquémicos, en general cardioembólicos, especialmente si el INR es infraterapéutico. Se pueden reintroducir ACO sin complicaciones, siendo el uso de NACO todavía escaso. A pesar de su ineficacia, la evolución es mejor si INR > 1,7 al inicio del ictus.

Introduction

Cardioembolic strokes, the most frequent type of ischaemic stroke in some epidemiological studies, account for 20% to 30% of the total.[1,2] They are associated with greater neurological impairment, higher rates of early mortality, and poorer functional outcome at discharge. As a result, this type of stroke has a great socio-economic impact.[3]

Prevention is based on oral anticoagulants (OAC), as shown in several clinical trials and meta-analyses; these agents reduce the risk of stroke by >60%,[4] even in patients aged over 75.[5,6]

However, traditional OACs (warfarin, acenocoumarol) have some limitations. Regular follow-up visits are necessary to maintain the international normalised ratio (INR) within the therapeutic range, which is only achieved in 60% to 70% of cases according to population-based studies.[7] Due to lack of adherence to treatment and drug-drug and food-drug interactions, patients taking OACs usually have below therapeutic levels[7] and are, as a result, at a greater risk of stroke.[8] In addition, OACs cause a number of complications, mainly haemorrhaging at different sites. As a result, the practice of prescribing these agents has been questioned.[9] Several tools have been developed to assess the risk of haemorrhage and the risks and benefits of OAC treatment. One example is the HAS-BLED score,[10] which has been shown to be the most useful, especially for assessing the risk of intracranial haemorrhages.[11,12]

The introduction of new oral anticoagulants (NOAC), which require no regular follow-up visits and are associated with a lower rate of interactions, may help optimise cardioembolic stroke prevention. Several clinical trials have shown that NOACs are as effective as OACs for preventing ischaemic events, besides which they cause fewer haemorrhagic complications.[13–16] However, their higher cost and the lack of specific antidotes make clinicians hesitate to prescribe these agents.[17]

Our purpose was to analyse stroke aetiology, treatment effectiveness, and progression (especially in terms of INR values during the acute phase) of a cohort of patients experiencing an ischaemic stroke despite OAC treatment.

Patients and methods

We retrospectively reviewed the records of 1014 patients admitted to our neurology department with a diagnosis of ischaemic stroke during a 3-year period (2011—2013). Of these, we analysed the patients who were being treated with OACs at stroke onset (107 patients, 10.6%). All these patients showed good treatment compliance according to their relatives.

For each patient, we gathered the following epidemiological variables: sex; age; cardiovascular risk factors (CVRF: smoking, arterial hypertension, diabetes mellitus, dyslipidaemia); presence of emboligenic heart disease; scores on the $CHADS_2$,[18] CHA_2DS_2-VASc,[19] and HAS-BLED scales; duration of OAC treatment; INR during the acute phase; aetiology (TOAST[20] criteria); and topographical location (Oxfordshire Community Stroke Project classification[21]). We