IFR 114 IMPRT Institut de Médecine Prédictive et de Recherche Thérapeutique

EA 1046

Characteristics of patients exposed to oral anti-coagulant in a stroke hospital-based cohort

Centre Hospitalier Régional Universitaire de Lille

Université Lille Nord de France

J. Béné[1,2], S. Gautier[1,2], F. Richard[3], D. Leys[4], C. Cordonnier C[4], R. Bordet[1,2], J. Caron[1,2]

[1] *Lille Regional Pharmacovigilance Center, France*

[2] *EA1046, University of Lille 2, Medicine Faculty, France*

[3] *Inserm, UMR 744, University of Lille 2, Institut Pasteur de Lille, France*

[4] *Neurology Department, Lille, France*

INTRODUCTION & OBJECTIVES

- Ischemic events and intracranial hemorrhages are feared complications of atrial fibrillation and of antithrombotic treatment in such patients.
- The aim of this study was to describe, in a stroke hospital-based cohort, patients previously treated with vitamin K antagonists and to identify in those patients factors associated with stroke occurring.

METHODS

- This study was conducted in patients admitted in the stroke unit of Lille University Hospital and involved in the Biostroke cohort.
- Biostroke is a prospective cohort conducted between June 2005 and April 2009, with a three years of follow-up, where patients are included in the 48h following hemorrhagic, ischemic stroke or transient ischemic attack.
- Statistical analysis was carried out using SAS 9.1® software (SAS Institute, South Carolina, USA). To determine the factors associated with the stroke, we conducted logistic regression where variables with a *p*-value <0.2 in bivariate analysis were included in the multivariate model. Results were presented with odds ratio (OR) and 95% confidence interval (95% CI).

RESULTS

- Four-hundred and nine patients with hemorrhagic or ischemic stroke were selected in the Biostroke cohort (**Table 1**).
- Twenty-seven patients were treated with vitamin K antagonist before stroke, of which 23 by fluindione and 4 by warfarine.
- Comparison of baseline characteristics between patients treated with oral anticoagulants and patients not treated showed that patients treated were older (*p*=0.0005), presented more frequently arterial hypertension (*p*=0.03), heart failure (*p*=0.02), and atrial fibrillation (*p*<0.001) than patients not treated.
- Patients treated with oral anticoagulant presented more frequently intracranial haemorrhage and less frequently ischemic stroke than patients not exposed. Ischemic stroke was more frequently from cardioembolic origin in patients treated with oral anticoagulants.
- Mortality rate, NIHSS, Barthel scale and MMS score at 3 months of follow-up after the stroke were comparable in both groups.
- In a second step (**Table 2**), intracranial hemorrhage *vs* ischemic stroke were compared. The following variables were highly associated with intracranial hemorrhage in the univariate model: vitamin K antagonist exposure, stroke severity (NIHSS≤6 *vs* NIHSS>6), and alcohol consumption.

In the final multivariate model, intracranial haemorrhage (*versus* ischemic stroke) was independently associated with more severe stroke (NIHSS score <6) (OR: 0.26; 95% CI: 0.11-0.61), alcohol consumption (OR: 2.79; 95% CI: 1.29-6.02) and vitamin K antagonist exposure (OR: 2.98 ; 95% CI: 1.10-8.28).

Table 1. Population characteristics in patients treated or not with VKA

Variables	Values	Vitamine K antagonist exposure		
		Yes	No	
		27 (6.6%)	382 (93.4%)	*p*
Age, years, mean ± sd	67 ± 15	76,2 ± 10,9	66,6 ± 14.8	**0.0005**
Male gender, n (%)	217 (53.1)	13 (48.2)	179 (46.9)	0.89
Weight, kg, med [min-max]	70 [22-94]	80 [48-110]	74 [40-148]	0.29
Reason for admission				**0.02**
Ischemic stroke, n (%)	370 (90.5)	21 (77.8)	349 (91.4)	-
Atherosclerotic origin, n (%)	64 (15.6)	0 (0)	64 (16.8)	**0.02**
Cardioembolic origin, n (%)	121 (29.6)	16 (59.3)	105 (27.5)	**0.0005**
Intracranial hemorrhage, n (%)	39 (9.5)	6 (22.2)	33 (8.6)	-
Vitamine K antagonist exposure, n (%)	27 (6.6)	-	-	-
Fluindione, n (%)	23 (85.2)	-	-	-
Warfarine, n (%)	4 (14.8)	-	-	-
Arterial hypertension, n (%)	253 (61.8)	22 (81.5)	231 (60.4)	**0.03**
Diabetes, n (%)	79 (19.3)	8 (29.6)	71 (18.6)	0.22
Hypercholesterolemia, n (%)	186 (45.5)	16 (59.3)	170 (44.5)	0.13
Hypertriglyceridemia, n (%)	64 (15.7)	3 (11.1)	61 (16.0)	0.50
Smoker, n (%)	121 (29.6)	4 (14.8)	117 (30.6)	0.08
Alcohol consumption, n (%)	67 (16.4)	2 (7.4)	65 (17.1)	0.41
Atrial fibrillation, n (%)	71 (17.4)	20 (74.1)	51 (13.4)	**<0.0001**
Prothrombine time, %, med [min-max]	95 [86-100]	61 [39-70]	95 [87-100]	**<0.0001**
Follow up at 3 months				
Mortality, n (%)	33 (8.9)	0 (0)	33 (9.5)	0.13
NIHSS score, med [min-max]	1 [0-5]	0.5 [0-3.5]	1 [0-5]	0.53
Barthel score, med [min-max]	100 [70-100]	80 [65-100]	100 [70-100]	0.07
Rankin scale, med [min-max]	1 [0-3]	2 [0-4]	1 [0-3]	0.33
MMS, med [min-max]	29 [25-30]	28 [24-30]	29 [25-30]	0.79
INR, med [min-max]	1.4 [0.8-4.9]	1.4 [0.8-4.9]	-	-

Table 2. Comparison of baseline characteristics between patients with ischemic stroke and intracranial hemorrhage

Variables	Intracranial hemorrhage	Ischemic stroke	Univariate analysis		Multivariate analysis	
	n = 39	n=370	Odds Ratio (95% CI)	*p*	Odds Ratio (95% CI)	*p*
NIHSS<6 *vs* NIHSS≥6, n (%)	7 (18.0)	174 (47.0)	0.25 [0.11-0.57]	**0.001**	0.26 [0.11-0.61]	**0.002**
Alcohol consumption, n (%)	12 (30.8)	55 (15.0)	2.53 [1.21-5.29]	**0.01**	2.79 [1.29-6.02]	**0.009**
VKA exposure, n (%)	6 (15.4)	21 (5.7)	3.02 [1.14-8.01]	**0.03**	2.98 [1.10-8.28]	**0.04**
Stroke history, n (%)	7 (17.9)	42 (11.4)	1.70 [0.71-4.10]	0.23	-	-
Atrial fibrillation, n (%)	4 (10.3)	67 (18.1)	0.52 [0.18-1.50]	0.23	-	-
Age, years, mean ± sd	68.6 ± 14.9	67.1 ± 14.8	1.01 [0.98-1.03]	0.58	-	-
Prothrombine time, %, med [min-max]	93 [84-100]	95 [86-100]	0.99 [0.97-1.02]	0.81	-	-
Smoker, n (%)	11 (28.2)	110 (29.7)	0.93 [0.45-1.93]	0.84	-	-
Arterial hypertension, n (%)	24 (61.5)	229 (61.9)	0.98 [0.50-1.94]	0.97	-	-

DISCUSSION

This analysis was performed in an observational cohort of patients, which confirms data of vitamin K antagonist exposure in general population (more than 5% after 65 years old).

Intracranial haemorrhage was more frequent in cases of vitamin K antagonist exposure, which was confirmed in literature data where the occurrence of intracranial hemorrhage is more often linked to specific predisposing conditions of the patients and interaction with vitamin K antagonist than to a high anticoagulation intensity (Palareti et al. Chest 2014.)

This database presents however few limitations: exposure (short onset are well known risk factor), dose and observance to drugs are not available and the low number of vitamin k antagonist exposure represents a loss of power for the analysis.

CONCLUSION

These data suggest that stroke occurring in patients previously treated with oral anticoagulants concern older patients, with arterial hypertension and atrial fibrillation and are more frequently haemorrhagic, from cardioembolic origin in case of ischemic stroke compared to patients not treated.

Moreover patients with alcohol consumption, and vitamin K antagonist intake are independent risk factors for intracranial hemorrhage *vs* ischemic stroke. Moreover, high stroke severity was also associated with intracranial hemorrhage.