Preadmission statins treatment in stroke patients: opportunity to treat high vascular risk patients

J. Carneado-Ruiz [a], J. Sánchez-Payá [b], A. Alfaro-Sáez [a], M. Lezcano-Rodas [a], L. Berenguer-Ruiz [a], F. Mira-Berenguer [a], N. López-Hernández [a], A. García-Escrivá [a], J.M. Moltó-Jordà [a], F. Gracia-Fleta [a]

PREADMISSION STATINS TREATMENT IN STROKE PATIENTS: OPPORTUNITY TO TREAT HIGH VASCULAR RISK PATIENTS

Summary. Aim. *To describe the use of preadmission statins in patients with cerebrovascular accident and the possible predictive factors.* Patients and methods. *Cross-sectional observational study of 795 consecutive patients with acute cerebrovascular accident. We assessed the differences among patients who were on preadmission statins (161) and those who were not (634), regarding vascular risk factors and clinical and neurosonological atherothrombotic disease markers. For univariate analysis, we used squared chi test, and for multivariate analysis, logistic regression analysis.* Results. *Preadmission statins were 20.3%. In high vascular risk patients defined based on National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III), this reached 28% and it might be 72%. Predictive factors for preadmission statins use were, in a positive sense, the antecedent of hypercholesterolemia diagnosis (OR = 189; 95% CI = 58-615;* $p \leq 0.001$*) and stroke (OR = 2.1; 95% CI = 1.2-3.6;* $p \leq 0.01$*), and in a negative sense, smoking (OR = 0.38; 95% CI = 0.18-0.81;* $p = 0.012$*).* Conclusions. *In our population of patients with stroke, the predictive factors of preadmission statins did not adjust to the current therapeutic NCEP-ATP III recommendations; treatment with statins in high vascular risk population was way below the indications, it was 28% and it might be 72%. [REV NEUROL 2007; 45: 449-55]*

Key words. *Guidelines. Hypercholesterolemia. Predictor. Statins. Stroke. Stroke-unit. TIA.*

INTRODUCTION

Statins –inhibitors of the 3-hydroxy-3-methylglutaryl-coenzyme A (HMGCoA-reductase)– are useful in the primary prevention of stroke [1], and involve a decrease in the relative risk of this condition of 21% in patients with coronary heart disease (CHD) and CHD equivalent. Recently, its usefulness in the secondary prevention of ischemic stroke in absence of a history of CHD has also been demonstrated [2]. It is an effective treatment that is also cost-effective. [3]

The main issue with the efficiency of this treatment is its low percentage of use, both in CHD patients and in those clinical situations that are equivalent, such as peripheral arteriopathy and stroke. It is used only in around 30% of the patients where it would be indicated [4-12].

It is a known fact that the therapeutic recommendations stated in guidelines are not followed [4]. And in the case of statins, the factors determining its real use are not well known.

As recommended in National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) in patients with CHD or a CHD risk equivalent, LDL-lowering drug therapy can be started simultaneously with dietary therapy if the LDL level warrants. And the target LDL-C level considered for this population is < 100 mg/dL [13].

Data about the frequency of preadmission statins and the factors that predict its use in patients who suffered from stroke (who are the subgroup of risk patients where the stroke could not be prevented) are needed. This kind of work may help to identify those patients who are not treated and those factors influencing the decision not to treat. Identifying the factors determining this treatment would help change those ones that are modifiable. This may lead to improve stroke prevention and treatment.

AIMS

The aims of this study are: 1) to determine the frequency of preadmission statins use in stroke patients admitted to a tertiary care Hospital; 2) to study the possible variables that may predict its use.

PATIENTS AND METHODS

Patients characteristics and inclusion/exclusion criteria

This is a cross-sectional observational study. Data are prospectively collected. The population studied included patients with acute cerebrovascular accident. The representative sample of this population consisted of patients consecutively admitted due to this reason in our Stroke Unit. We studied the period of time from April 2002 to March 2005.

Inclusion criteria were: consecutive patients with acute cerebrovascular accident; ischemic stroke was defined as a sudden focal neurological deficiency, persisting for more than 24 hours (or causing the patient's death during this period), documented by a cranial CAT scan or a cranial MRI indicating the presence or absence of intracranial hemorrhage [14]. The transient ischemic attack (TIA) was defined as a focal neurological deficit possibly due to brain ischemia of a duration of less than 24 hours [15]. A patient suffering from a relapsing episode of ischemic stroke was considered as a new event, and was included as such in the analysis.

The exclusion criteria considered were: lipid profile was not systematically done at admission in every patient. We considered as a exclusion criteria the lack of information in the database regarding complete lipid profile. We considered the patient to have a complete lipid profile when at least total cholesterol and LDL-cholesterol (LDL-C) were determined. The studied

Accepted: 25.09.07.

[a] Stroke Unit. Neurology Department. [b] Preventive Medicine Department. Hospital General Universitario de Alicante. Alicante, Spain.

Corresponding author: Dr. Joaquín Carneado Ruiz. Unidad de Ictus. Servicio de Neurología. Hospital General Universitario de Alicante. Sinesio Delgado, s/n. E-08010 Alicante. E-mail: jcarnead@hotmail.com

Versión española disponible en www.neurologia.com

variables are gathered in a prospective register, where the clinical and laboratory variables are recorded, as well as the variables related with the neurosonologic findings. Our hospital's Research Project Evaluation Committee approved the study.

Study of variables

The independent variable studied was preadmission statins. The dependent variables studied were:

Related to the subject: age, sex, vascular risk factors defined as high blood pressure (HBP) [16], diabetes mellitus (DM) [17], hypercholesterolemia [18], active smoker –number of cigarettes not stated–, consumption of alcohol [19].

History of atherothrombotic disease: history of previous ischemic stroke [14] or TIA [15]. Personal history of CHD [20]. Personal history of peripheral arteriopathy, defined as: history of intermittent claudication, disease documented with the Doppler study or a history of revascularisation surgery.

High vascular risk patient: patients with CHD or CHD equivalent (symptomatic carotid atherosclerosis, symptomatic peripheral arterial atherosclerosis or diabetes) as defined in NCEP-ATP III, we didn't include multiple risk factors and 10-year probability of CHD > 20% patients because we couldn't calculate it with exactitude (the family history of premature CHD, and a basal measured of systolic blood pressure are lacking at our database) [13].

Patients that might have preadmission statins treatment are defined as: high vascular risk patients with LDL-C ≥ 100 mg/dL.

Related to ischemic stroke: aetiology of the ischemic stroke according to Lausanne criteria [21]; atherothrombotic or other aetiology of the TIA applying the Lausanne classification criteria [21], classification of the ischemic stroke according to the Oxfordshire Community Stroke Project (OCSP). Symptomatic arterial stenosis was defined as stenosis with a corresponding clinical syndrome and confirmed by magnetic resonance imaging in DWI sequence. NIHSS score at admission. Temperature at admission.

Related to the neurosonology study, we rated the degree of carotid atherothrombotic disease with one of the following three categories: atheromatous plaque with 50% stenosis of the internal carotid artery, atheromatous plaque without 50% stenosis of the internal carotid artery, and no atheromatous plaque. And we considered the highest degree of atherothrombotic disease in both carotid arteries, i.e. if one patient had a ≥ 50% stenosis in one of the carotids, that was the degree of disease considered for that patient. We considered the existence of a stenosis of the intracranial artery, and also the fact that a patient had arterial stenosis or not, either extra- or intracranial.

Table I. Cerebrovascular accident LDL-C determined group and non LDL-C determined group differences.

	Patients included: LDL-C determined (*n* = 795) *n* (%)	Patients excluded: LDL-C non determined (*n* = 221) *n* (%)	*p*
Age ≤ 75 years-old	451 (56.9)	117 (53.4)	0.35
Male	416 (52.5)	108 (49.3)	0.42
High blood pressure	508 (63.9)	149 (67.4)	0.34
Diabetes mellitus	270 (34)	86 (38.9)	0.17
Hypercholesterolemia	293 (36.9)	85 (30.5)	0.35
Smoker	134 (19.4)	48 (21.7)	0.44
Alcohol	61 (7.7)	12 (5.4)	0.25
CHD antecedent	83 (10.5)	29 (13.1)	0.26
CVA antecedent	228 (28.7)	75 (33.9)	0.13
PAD antecedent	36 (4.5)	11 (5)	0.7
CHD and equivalent [a]	397 (50.1)	113 (51.1)	0.77
NIHSS ≥ 4	384 (49.4)	100 (46.5)	0.45
CRP ≥ 1.5 mg/dL	119 (25.9)	28 (35)	0.09
TS	161 (20)	31 (14)	0.03
Symptomatic TS	112 (14.2)	27 (12.3)	0.5
CS ≥ 50%	122 (15.3)	25 (11.3)	0.15
Symptomatic CS ≥ 50%	87 (11)	20 (9.1)	0.45
IS	46 (5.8)	9 (4.1)	0.4
Symptomatic IS	24 (3)	7 (3.2)	0.9
Carotid atheromatous plaque	494 (63.7)	130 (61.3)	0.5
Atherothrombotic CVA	278 (35)	79 (35.7)	0.83
Atherothrombotic TIA	101 (16.3)	34 (19.3)	0.35
Atherothrombotic stroke	177 (25.5)	45 (24.1)	0.68
Statins antecedent	154 (19.4)	48 (21.7)	0.43

[a] NCEP-ATP III based definition. CHD: coronary heart disease; PAD: peripheral artery disease; CVA: cerebrovascular accident; CRP: C-reactive protein; TS: total arterial stenosis; CS: carotid artery stenosis; IS: intracranial artery stenosis; TIA: transient ischemic attack.

Study protocol

The study and treatment of the stroke was carried out following a protocol that included a detailed clinical history, collected in a semi-structured fashion, and an exhaustive neurological examination. The laboratory tests included complete blood count, erythrocyte sedimentation rate (ESR), BUN, creatinine, total cholesterol, LDL-C and HDL-C fractions, triglycerides, glucose, electrolytes, hepatic enzymes, 12-lead electrocardiogram (conducted periodically if arrhythmia was suspected), chest X-ray, cranial CAT scan at admission, and another cranial CAT scan or MRI in day 3-5. A neurosonology study, including duplex ultrasonography of the supra-aortic arteries and transcranial Doppler, was conducted in all patients in the first 48 hours. When the suspicion of cardioembolic aetiology indicated it, a transthoracic and transoesophagic ecocardiography was obtained, a 24-hour Holter ECG was also deemed indicated, as well as thrombophilic, immunologic and serologic studies (syphilis, Lyme's disease and HIV) if deemed opportune by the attending neurologists.

The degree of the neurological deficit was assessed by means of the National Institutes of Health Stroke Scale (NIHSS), Barthel and Rankin indexes at admission and at discharge, or at 7 days and 90 days. The clinical work of the Stroke Unit was developed and conducted by neurologists, especially involved in cerebrovascular diseases (GFF, MJJM, CRJ), the neurosonology study being conducted by two of them with a special training and expertise in these techniques (MJJM, CRJ) following a study protocol and taking into account the previously published criteria [22-24].

Statistical methods

First, the patients included in the study were compared with those not included due to lack of a complete lipid profile. A description of the clinical features of the patients included was made, by calculating the absolute and relative frequencies, in percentage, of each of the variables values. Then the association between the patients' clinical characteristics and the preadmission use of statins was studied using the chi squared test; to quantify the magnitude of the association, the odds ratios (OR) were calculated along

Table II. Patients clinical characteristics (n = 795).

Mean age (SD)	71.4 (12.1)
Male (%)	416 (52.3)
Basal NIHSS median (range)	4 (0-27)
LDL-C ≥ 100 mg/dL (%)	582 (73.3)
Total cholesterol > 200 mg/dL (%)	354 (44.6)
Triglycerides ≥ 150 mg/dL (%)	234 (29.4)
HDL-C > 60 mg/dL (%)	162 (20.6)
HDL-C < 40 mg/dL (%)	175 (22)
Laussanne Stroke Diagnosis Criteria	
Non atherothrombotic TIA (%)	75 (9.4)
Atherothrombotic TIA (%)	101 (12.7)
Atherothrombotic stroke (%)	177 (22.3)
Cardioembolic stroke (%)	127 (16)
Lacunar stroke (%)	229 (28.8)
Rare cause stroke (%)	8 (1)
Undetermined stroke (%)	78 (9.8)
OCSP diagnosis	
LACI (%)	259 (32.6)
PACI (%)	194 (24.4)
TACI (%)	64 (8.1)
POCI (%)	91 (11.4)
Undetermined (%)	187 (23.5)

OCSP: Oxfordshire Community Stroke Project; TIA: transient ischemic attack.

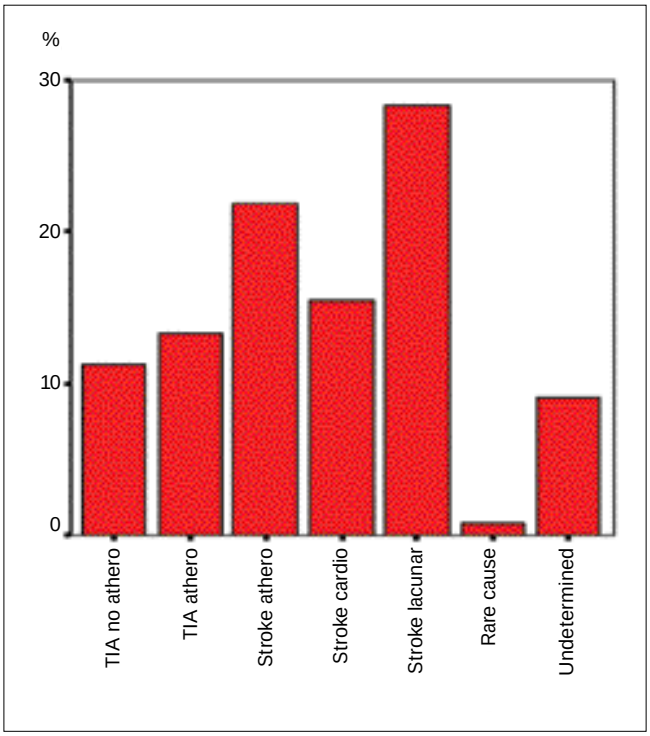

Figure 1. Cerebrovascular accident subtypes distribution. TIA: transient ischemic attack; athero: atherothrombotic; cardio: cardioembolic.

with their 95% confidence intervals (95% CI); then, a multivariate logistic regression analysis was conducted with those variables who were significant in the bivariate analysis, in order to determine the independent effect of each of these variables. In all hypothesis contrasts, the significance level used was $p < 0.05$. The software used for the statistical analysis of the data was SPSS v. 10.1.

RESULTS

Study of the possible selection biases

We studied a sample of 1,016 patients with ischemic stroke. After the study exclusion, 795 patients were eligible. We excluded 221 patients (21.7%) the reason was that the LDL-C value was missing. To study the possibility of selection biases, we analysed the differences between the sample studied with a complete lipid profile and the group of excluded patients (Table I). The only difference we found was a higher percentage of arterial stenosis among the patients with a complete lipid profile study with OR = 1.57 (95% CI = 1.03-2.38; $p = 0.03$). We did not find significant differences among the rest of variables studied.

Patients' clinical characteristics

The descriptive general study is shown in tables I and II. The value expressed as mean and standard deviation (SD) of some variables not included in the table was: temperature 36.2 ºC (SD: 0.56), ESR 31.2 mm (SD: 20.7), total cholesterol 196 mg/dL (SD: 46), LDL-C 126 mg/dL (SD: 41), HDL-C 50 mg/dL (SD: 14), triglycerides 135 mg/dL (SD: 76); the antithrombotic therapy used by the patients was: AAS 120 (15.1%), clopidogrel 63 (7.9%), and sintrom 53 (6.7%).

There were 22 re-admissions due to recurrence of ischemic stroke (a patient had 2 re-admissions), totalling 2.76% of the sample.

The value of the discharge score in the evaluation scales (median and range) was: NIHSS at discharge 2 (0-42), Barthel at discharge 95 (0-100), Rankin at discharge 1 (0-6).

The distribution by type of preadmission statin taken was: atorvastatin 44 (5.5%), pravastatin 25 (3.1%), simvastatin 57 (7.2%), fluvastatin 5 (0.6%), lovastatin 2 (0.3%), unknown 20 (2.5%).

Regarding the distribution of the clinical diagnosis and OCSP, they are described in tables I and II and figure 1. The distribution of undetermined origin ischemic stroke was: undetermined due to incomplete study 13 (1.6%), due to coincident causes 29 (3.6%) and undetermined after a thorough study (4.5%).

The types of arterial stenosis diagnosed are described in table I.

High vascular risk patients: 397 patients (49.9%). Stroke patients that might have preadmission statins treatment: 288 high vascular risk patients had values of LDL-C ≥ 100 mg/dL (36.2% of total stroke sample and 72% of high vascular risk patient subgroup).

Analysis of preadmission statins used in patients with ischemic stroke

In our population, preadmission statins were used by 20.3%. Preadmission statin treatment in the subgroup of high vascular risk patients were followed by 112 patients (28%).

In the rest, the distribution was the following: In patients with a history of hypercholesterolemia 158 (53%), HBP 127 (25%), DM 82 (30%), CHD 34 (40%), ischemic stroke 65 (28%), peripheral arteriopathy 12 (33%), carotid atheromatous plaque 116 (23 %).

The proportion of patients taking preadmission statins in each subtype of stroke was (Fig. 2): in those patients with atherothrombotic TIA 20 (12.4%), TIA without atherothrombotic origin criteria 5 (3.1%), atherothrombotic stroke 43 (26.7%), cardioembolic stroke 26 (16.1%), lacunar stroke 50 (31.1%), rare cause stroke 0 (0%), undetermined 17 (10.6%).

In our study, of the patients who were following a previous treatment with statins, 45 (27.9%) had the recommended goal LDL-C levels < 100 mg/dL. There was no association between both variables ($p = 0.68$).

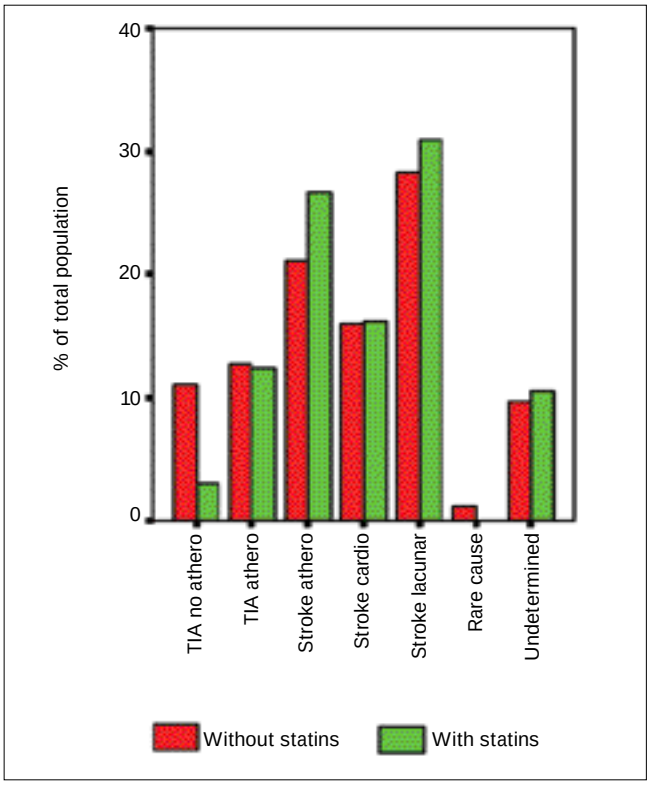

Figure 2. Preadmission statins treatment distribution in cerebrovascular accident subtypes. TIA: transient ischemic attack; athero: atherothrombotic; cardio: cardioembolic.

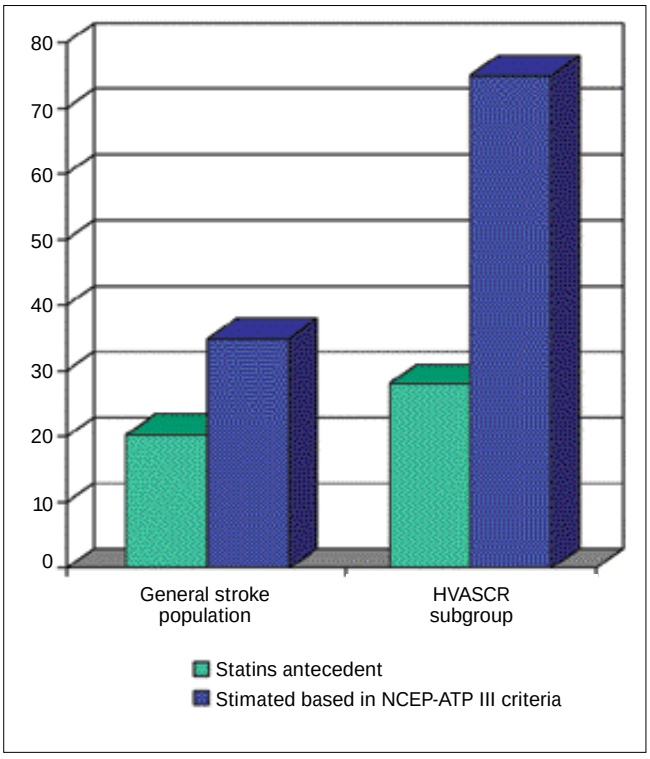

Figure 3. Preadmission statins treatment distribution in our serie and stimated based in NCEP-ATP III criteria in general stroke population and the high vascular risk subgroup. HVASCR: high vascular risk subgroup.

Analysis of predictors of preadmission statins used

The difference between the group taking statins and the group who did not is shown in table III.

When applying the logistic regression multivariate analysis to obtain the adjusted OR, the following were found to be independent factors: a history of hypercholesterolemia and stroke, with a positive sign, and being smoker, with a negative sign.

DISCUSSION

Conducting a complete lipid profile at admission of the patient with stroke

In our series, the total cholesterol in the first 48 hours was determined in 891 patients (87.6%), and the complete lipid profile in 795 (78%). Recent stroke studies show that less than 50% of the patients have their cholesterol level studied [5]. The only factor predicting the complete lipid profile in our patients with stroke is the diagnosis of arterial stenosis. This seems to indicate that the degree of atherothrombosis evaluated and expressed objectively acts as a positive stimulus to conduct the complete study. We did not find differences in age, sex or the rest of variables.

In the remaining studies published, the complete lipid profile is more frequently determined in patients aged 50 to 69 years [5,6], and to a lesser extent, in women [25].

Preadmission statins use

In our study, 20.3 % of the patients with ischemic stroke were taking statins in the preadmission . They might be 36.2% of the whole population as was calculated based on NCEP-ATP III. This difference is marker in the subgroup defined as high vascular risk patients, they actually have a preadmission use of 28% and it might be 72% (Fig. 3). The ones on statins correspond mainly to patients with a history of hypercholesterolemia , but the high vascular risk added to LDL-C level ≥ 100 mg/dL criteria recommended in NCEP-ATP III were ignored. Our data are similar to those of other series of patients with stroke in other contexts and countries. Those described a lower use of preadmission statins than are expected after the actual recommendations, which ranges from 10% to 43% [5,7-9].

In the published series, the reported percentage of patients with stroke where statins are indicated after discharge is also usually low. Thus, 68% of the patients with stroke and clinically relevant atherothrombosis and hypercholesterolemia were not treated with statins after discharge [15]. Contrary in our series, we treated with stains after discharge 57% of ischemic stroke patients.

The low frequency of statin use in stroke is comparable to the one found in CHD, which ranges from 30% to 37% of the population [4,10]. In patients with peripheral arteriopathy, the reported use of statins ranges from 5% to 35% [22,23].

Inadequate level of LDL-C according to therapeutic recommendations

73.3 % of our patients have levels of LDL-C ≥ 100 mg/dL. In other series of patients with stroke, the reported percentage of patients with LDL-C ≥ 100 mg/dL is 58%-80% [7,9].

In patients with high vascular risk, the recommended therapeutic target for primary prevention of stroke is a level of LDL-C < 100 mg/dL [1]. In our series, the percentage of patients with high LDL-C in this subgroup was 72%. In another published se-

Table III. Predictors of statins antecedent.

	Preadmission statins (*n* = 161) *n* (%)	Non preadmission statins (*n* = 634) *n* (%)	ORc (CI 95%)	*p*	ORa (CI 95%)	*p*
Age ≥ 75 years-old	57 (35.4)	284 (45)	0.67 (0.46-0.95)	0.028	0.71 (0.39-1.27)	0.25
Male	84 (52.2)	332 (52.6)	1.01 (0.72-1.43)	0.92		
High blood pressure	127 (78.9)	381 (60.1)	2.48 (1.64-3.73)	< 0.001	1.7 (0.94-3.07)	0.07
Diabetes mellitus	82 (50.9)	188 (29.7)	2.46 (1.73-3.5)	< 0.001	0.73 (0.31-1.68)	0.46
Hypercholesterolemia	158 (98.1)	135 (21.3)	194 (61-619)	< 0.001	189 (58-615)	< 0.001
Smoker	18 (11.2)	130 (20.5)	0.48 (0.28-0.82)	0.006	0.38 (0.18-0.81)	0.012
Alcohol	6 (3.7)	55 (8.7)	0.40 (0.17-0.96)	0.035	0.4 (0.13-1.25)	0.11
CHD antecedent	34 (21.3)	49 (7.7)	3.21 (1.99-5.18)	< 0.001	1.17 (0.51-2.65)	0.69
CVA antecedent	65 (40.4)	163 (25.8)	1.95 (1.36-2.8)	< 0.001	2.1 (1.2-3.6)	< 0.01
PAD antecedent	12 (7.5)	24 (3.8)	2.04 (1 -4.18)	0.046	1.31 (0.41-4.04)	0.64
CHD and equivalent [a]	112 (70)	285 (45)	2.84 (1.96-4.13)	< 0.001	2.27 (0.91-5.66)	0.07
NIHSS ≥ 4	83 (53.3)	301 (48.4)	1.22 (0.86-1.74)	0.25		
LDL-C ≥ 100mg/dL	116 (72)	466 (75.6)	0.92 (0.62-1.36)	0.68		
Total cholesterol ≥ 200 mg/dL	72 (44.7)	282 (44.5)	1 (0.85-1.17)	0.96		
Tryglicerides ≥ 150 mg/dL	92 (59.7)	429 (71.4)	0.59 (0.41-0.85)	0.005	0.77 (0.54-1.57)	0.77
HDL-C > 60 mg/dL	29 (18)	133 (21.2)	0.81 (0.52-1.27)	0.37		
HDL-C < 40 mg/dL	36 (22.4)	139 (21.9)	1.02 (0.67-1.55)	0.91		
CRP ≥ 1.5 mg/dL	29 (28.7)	90 (25.1)	1.2 (0.73-1.97)	0.46		
TS	38 (33.9)	123 (19.6)	1.29 (0.85-1.95)	0.22		
Symptomatic TS	29 (18.1)	83 (13.2)	1.45 (0.91-1.32)	0.1		
CS ≥ 50%	32 (19.9)	90 (14.2)	1.49 (0.95-2.34)	0.07		
Symptomatic CS	23 (14.4)	64 (10.2)	1.48 (0.89-2.41)	0.12		
IS	9 (5.7)	37 (5.9)	0.96 (0.45-2.03)	0.91		
Symptomatic IS	6 (3.7)	18 (2.8)	1.32 (0.51-3.39)	0.55		
Carotid atheromatous plaque	116 (73.4)	378 (61.3)	1.74 (1.18-2.57)	0.005	0.66 (0.37-1.18)	0.16
Atherothrombotic CVA	63 (39.1)	215 (33.9)	1.25 (0.87-1.79)	0.21		
Atherothrombotic TIA	20 (12.4)	81 (12.8)	1.05 (0.61-1.80)	0.84		
Atherothrombotic stroke	43 (26.7)	134 (21.1)	1.37 (0.91-2.06)	0.91		

[a] NCEP-ATP III based definition. ORc: crude odds ratio; ORa: adjusted odds ratio; CHD: coronary heart disease; PAD: peripheral artery disease; CVA: cerebrovascular accident; CRP: C-reactive protein; TS: total arterial stenosis; CS: carotid artery stenosis; IS: intracranial artery stenosis; TIA: transient ischemic attack.

ries, a percentage of 39%-63% was reported [7,8] Patients with CHD equivalents and LDL target < 100 mg/dL were most likely to fail to be at goal [8]

Of those patients following a previous treatment with statins, 72.1% had an inadequate level of LDL-C. In another published series, a percentage of 42% was reported [7].

Frequently, an adequate level of LDL is not achieved in everyday clinical practice [4]. In single centre studies it is shown that control of dyslipidaemia after a stroke is insufficient, either the correct treatment is not started or it is done inadequately, and the established therapeutic target is not reached [27].

Multivariate analysis to identify predictive factors of preadmission statins

A relevant independent predictor of the use of statins was the antecedent of hypercholesterolemia diagnosis; variables related to high vascular risk and LDL-C level ≥ 100 mg/dL reflecting the essence of NCEP-ATP III [13] were not significant; another factor that was not predictive of preadmission statins was the degree of carotid atherothrombotic disease, defined as arterial stenosis or the presence of atheromatous plaques.

The other factor predicting the use of statins for the positive sense is a previous ischemic stroke, probably due to the influ-

ence of being previously cared for at a stroke unit [28]. The history of smoking is associated to a lower probability of being prescribed statins, which probably reflects the fact that smokers do not follow controls nor medical recommendations in general.

We have to inform about patients at atherothrombosis risk undertreated with statins as we do with atrial fibrillation and low therapeutic goals with anticoagulation treatment [29].

The limitations of our study are the usual ones in a cross-sectional study, i.e., the study does identify associations, but not causes; a prospective study should be designed instead.

This is a single center study, but the main results are comparable to the other series published, included inadequate LDL-C goal attained in high vascular risk patients, so probably, the fact that this subgroup is highly undertreated could be a generalized phenomenon.

Twenty two percent of the stroke patients were not eligible due to a missing complete lipid profile; excluded subjects were comparable in terms of age, sex, vascular risk factors and subtype of cerebrovascular accident. There was only a difference in the number of patients with arterial stenosis, which does not influence on the analysis result nor in the conclusions drawn from the study. Thus, we believe that the selection bias was not an obstacle for our study. On the other hand, as we have stated before, it is a cross-sectional study with a good design within a Stroke Unit, with reproducible diagnostic criteria and therapeutic schedules, carried out in a stable hospital with a reference area of its own.

The design of the study respected the blinding of those in charge of assessing the clinical and neurosonologic variables, the laboratory test staff, and those responsible for the statistical analysis (SPJ).

In conclusion, the use of preadmission statins in our population of stroke patients was 20.3%, these are low figures, as we calculated based on NCEP-ATP III recommendations it might be 36.2%.

It occurred mainly in patients with high vascular risk criteria, the frequency of preadmission statins use in this subgroup was 28% and it might be 72%.

The main predictive factors for preadmission statins was hypercholesterolemia diagnosis but not the other criteria recommended in NCEP-ATP III related to vascular risk status and a lower LDL-C treatment goal.

REFERENCES

1. Amarenco P, Labreuche J, Lavallee P, Touboul PJ. Statins in stroke prevention and carotid atherosclerosis: systematic review and up-to-date meta-analysis. Stroke 2004; 35: 2902-9.
2. Amarenco P, Bogousslavsky J, Callahan A III, Goldstein LB, Hennerici M, Rudolph AE, et al. Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Investigators. High-dose atorvastatin after stroke or transient ischemic attack. N Engl J Med 2006; 355: 549-59.
3. Prosser LA, Stinnett AA, Goldman PA, Williams LW, Hunink MG, Goldman L, et al. Cost-effectiveness of cholesterol-lowering therapies according to selected patient characteristics. Ann Intern Med 2000; 132: 769-79.
4. Frolkis JP, Zyzanski SJ, Schwartz JM, Suhan PS. Physician noncompliance with the 1993 National Cholesterol Education Program (NCEP-ATP II) guidelines. Circulation 1998; 98: 851-5.
5. Mullard AJ, Reeves MJ, Jacobs BS, Kothari RU, Birbeck GL, Maddox K, et al. Paul Coverdell National Acute Stroke Registry. Michigan Prototype Investigators. Lipid testing and lipid-lowering therapy in hospitalized ischemic stroke and transient ischemic attack patients: results from a statewide stroke registry. Stroke 2006; 37: 44-9.
6. Lalouschek W, Lang W, Greisenegger S, et al, Vienna Stroke Study Group. Determination of lipid profiles and use of statins in patients with ischemic stroke or transient ischemic attack. Stroke 2003; 34: 105-10.
7. Ovbiagele B, Saver JL, Bang H, Chambless LE, Nassief A, Minuk J, et al. VISP Study Investigators. Statin treatment and adherence to national cholesterol guidelines after ischemic stroke. Neurology 2006; 66: 1164-70.
8. Smith EE, Abdullah AR, Amirfarzan H, Schwamm LH. Serum lipid profile on admission for ischemic stroke: failure to meet National Cholesterol Education Program Adult Treatment Panel (NCEP-ATP III) guidelines. Neurology 2007; 68: 660-5.
9. Amarenco P, Labreuche J, Elbaz A, Touboul PJ, Driss F, Jaillard A, et al. Blood lipids in brain infarction subtypes. Cerebrovasc Dis 2006; 22: 101-8.
10. Fonarow GC, French WJ, Parsons LS, Sun H, Malmgren JA. Use of lipid-lowering medications at discharge in patients with acute myocardial infarction: data from the National Registry of Myocardial Infarction 3. Circulation 2001; 103: 38-44.
11. Nass C, Allen J, Jermyn R, Fleischer L. Secondary prevention of coronary artery disease in patients undergoing elective surgery for peripheral artery disease. Vasc Med 2001; 6: 35-41.
12. Hirsch AT, Criqui MH, Treat Jacobson D, Regensteiner JG, Creager MA, Olin JW, et al. Peripheral arterial disease detection, awareness, and treatment in primary care. JAMA 2001; 286: 1317-24.
13. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Final Report. Circulation 2002; 106; 3143-421.
14. Foulkes MA, Wolf PA, Price TP, Mohr JP, Hier DB. The Stroke Data Bank: design, methods, and baseline characteristics. Stroke 1988; 19: 547-54.
15. Genton E, Barnett HJ, Fields WS, Gent M, Hoak JC. Cerebral ischemia: the role of thrombosis and of antithrombotic therapy. Study group on antithrombotic therapy. Stroke 1977; 8: 150-75.
16. JNC VI. The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Arch Intern Med 1997; 157: 2413-46.
17. Gavin JR III, Alberti KGMM, Davidson MB, DeFronzo RA, Drash A, Gabbe SG, et al. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 1998; 21 (Suppl): S5-19.
18. National Cholesterol Education Program. Second report of the expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel II). Circulation 1994; 89: 1333-445.
19. Criqui MH. Alcohol and hypertension: new insights from population studies. Eur Heart J 1987; (Suppl B): S19-26.
20. The Joint European Society of Cardiology/American College of Cardiology Committee. Myocardial infarction redefined –a consensus document of the Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. Eur Heart J 2000; 21: 1502-13.
21. Bogousslavsky J, Van Melle G, Regli F. The Lausanne Stroke Registry: analysis of 1,000 consecutive patients with first stroke. Stroke 1988; 19: 1083-92.
22. Tegeler CH, Babikian V, Gómez CR, eds. Neurosonology. St. Louis: Mosby; 1996.
23. Handa N, Matsumoto M, Maeda H, Hougaku H, Kamada T. Ischemic stroke events and carotid atherosclerosis. Results of the Osaka Follow-up Study for Ultrasonographic Assessment of Carotid Atherosclerosis (the OSACA Study). Stroke 1995; 26: 1781-6.
24. Baumgartner RW, Mattle HP, Schroth G. Assessment of >/= 50% and < 50% intracranial stenoses by transcranial color-coded duplex sonography. Stroke 1999; 30: 87-92.
25. Kim C, Hofer TP, Kerr EA. Review of evidence and explanations for suboptimal screening and treatment of dyslipidemia in women. A conceptual model. J Gen Intern Med 2003; 18: 854-63.
26. Wolf PA, Clagett GP, Easton JD, Goldstein LB, Gorelick PB, Kelly-Hayes M, et al. Preventing ischemic stroke in patients with prior stroke and transient ischemic attack: a statement for healthcare professionals from the Stroke Council of the American Heart Association. Stroke 1999; 30: 1991-4.
27. Joseph L, Babikian VL, Allen NC, Winter MR. Risk factor modification in stroke prevention: the experience of a stroke clinic. Stroke 1999; 30: 16-20.
28. Ovbiagele B, Saver JL, Fredieu A, Suzuki S, Selco S, Rajajee V, et al. In-hospital initiation of secondary stroke prevention therapies yields high rates of adherence at follow-up. Stroke 2004; 35: 2879-83.
29. Deplanque D, Leys D, Parnetti L, Schmidt R, Ferro J, De Reuck J, et al. SAFE II Investigators. Stroke prevention and atrial fibrillation: reasons leading to an inappropriate management. Main results of the SAFE II study. Br J Clin Pharmacol 2004; 57: 798-806.

ANTECEDENTE DEL USO DE ESTATINAS EN EL ICTUS: OPORTUNIDAD DE MEJORA EN EL PACIENTE CON ALTO RIESGO VASCULAR POR ATEROTROMBOSIS

Resumen. Objetivos. *Describir el antecedente de uso de estatinas en los pacientes con ictus isquémico y sus posibles factores predictores.* Pacientes y métodos. *Estudio observacional transversal de 795 pacientes consecutivos con ictus isquémico. Evaluamos diferencias entre los pacientes con antecedente de uso de estatinas (161) y los que no lo tenían (634), en cuanto a factores de riesgo vascular y marcadores de enfermedad aterotrombótica clínicos y neuroecográficos. Utilizamos para el análisis univariante el test de chi al cuadrado y para el análisis multivariante los cálculos de regresión logística.* Resultados. *El antecedente de uso de estatinas fue de un 20,3%. En los pacientes con alto riesgo vascular definidos basados en criterios del* National Cholesterol Education Program Adult Treatment Panel III *(NCEP-ATP III) fue del 28% y debió ser del 72%. Los factores predictores del uso de estatinas fueron, en un sentido positivo, el antecedente de hipercolesterolemia (OR = 189; IC 95% = 58-615;* $p \leq 0{,}001$*) y de ictus (OR = 2,1; IC 95% = 1,2-3,6;* $p \leq 0{,}01$*), y en un sentido negativo, ser fumador (OR = 0,38; IC 95% = 0,18-0,81;* $p = 0{,}012$*).* Conclusiones. *En nuestra población de pacientes con ictus, los factores predictores del antecedente de uso de estatinas no se ajustaron a las recomendaciones terapéuticas actuales; el tratamiento con estatinas en la población con alto riesgo vascular estuvo muy por debajo de lo indicado, fue del 28%, debiendo alcanzar el 72% según el criterio NCEP-ATP III. [REV NEUROL 2007; 45: 449-55]*

Palabras clave. *Accidente isquémico transitorio. Estatinas. Guías clínicas. Hipercolesterolemia. Ictus. Infarto cerebral. Unidad de ictus.*