Ruiz_001-12.qxd 10/13/04 10:22 AM Page 1

ORIGINAL RESEARCH ARTICLE

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Current Lipid Management and Low Cholesterol Goal Attainment in Common Daily Practice in Spain

The REALITY Study

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Abstract

Objective: To evaluate prescribing patterns of lipid-lowering drugs used in management of patients at risk of coronary heart disease (CHD) in usual clinical practice in Spain and to assess low-density lipoprotein cholesterol (LDL-C) goal attainment among CHD and CHD equivalent patients (<100 mg/dL) and non-CHD patients with two or more risk factors (<130 mg/dL) who were prescribed lipid-lowering drugs.

Methods: Cohort study with retrospective chart review at 23 primary care centres and 16 lipid treatment centres across Spain (59% primary care; 41% outpatient lipid centres). Physicians consecutively identified eligible patients. Adults (aged ≥18 years) with CHD/CHD equivalent or two or more major risk factors prior to first prescription of lipid-lowering drugs were eligible. Medical records were reviewed by physicians to collect patient characteristics, baseline and follow-up laboratory values and lipid-lowering drug treatment data.

Results: 619 patients (45.5% CHD and CHD equivalent patients and 54.5% non-CHD with two or more major risk factors) were included in the study with an average study follow-up of 3.6 years. Mean age was 60.1 years (SD 10.2), and 47.8% were female. Mean baseline LDL-C was 178 mg/dL (SD 45.0) for the CHD/CHD equivalent patients and 191 mg/dL (SD 56.95) for patients with two or more risk factors. Statins were the initial lipid-lowering drugs in 90.2% of patients; 52.5% of patients were initiated on low-dose (simvastatin 10mg or lower potency) statins. Overall 20.2% of CHD/CHD equivalent and 31.4% of patients with two or more risk factors attained LDL-C goal during the study period; of patients not attaining goal, 28.7% required an additional LDL-C reduction of >30% to attain goal. In a logistic

Ruiz_001-12.qxd 10/13/04 10:22 AM Page 2

regression model for goal attainment, CHD/CHD equivalent patients (odds ratio [OR] 0.47; 95% confidence interval [CI] 0.31, 0.72) and patients with baseline LDL-C >190 mg/dL (OR 0.53; 95% CI 0.35, 0.80) were least likely to reach cholesterol goal when compared with patients having baseline LDL-C >100 mg/dL and <130 mg/dL.

Conclusion: Only 12.9% of patients attained LDL-C goal on their initial lipid-lowering drugs, and an additional 13.4% achieved goal after a change in their lipid-lowering therapy, resulting in 73.7% of patients not attaining goal after at least 3 years of follow-up, after initiation of lipid-lowering therapy. Patients who would gain the most from aggressive lipid lowering (CHD patients and patients with high baseline LDL-C) were least likely to achieve goal. More effective lipid management is needed to help these patients lower their cholesterol to goal levels or even lower.

Introduction

According to the World Health Organization's World Health Report 2003, cardiovascular disease is responsible for 13% of the disease burden among adults aged over 15 years (16.7 million deaths in 2002).[1] In developed countries, coronary heart disease (CHD) and cerebrovascular disease together account for 36% of all deaths.[1] In Spain too, cardiovascular disease ranks as the major cause of death, accounting for 34.5% of all deaths annually.[2]

Several epidemiological studies and randomised clinical trials have demonstrated that reducing cholesterol will reduce the number of CHD events.[3-9] Based on existing evidence, the National Cholesterol Educational Program (NCEP) Adult Treatment Panel III (ATP III) guidelines in the US, the European Joint Task Force, and the Spanish Ministry of Health have all specified target cholesterol levels (goals) for patients in different CHD risk categories and have recommended aggressive risk management and reduction of low-density lipoprotein cholesterol (LDL-C) in CHD patients and in non-CHD patients who are at elevated risk.[10-12] However, recent studies show that reducing cholesterol levels even below current guideline-specified goals provides substantial additional reduction in fatal cardiovascular events.[13]

In Spain, comparison of PREVESE I and PREVESE II, two cross-sectional studies of secondary prevention patients conducted in 1994 and 1998, respectively, indicated a trend of increased use of lipid-lowering drugs in general, and of statins specifically, in the management of myocardial infarction (MI) patients.[14,15] At the European level, a similar comparison between EUROASPIRE I (1995-1996) and EUROASPIRE II (1999-2000) demonstrates a similar increase in the use of lipid-lowering drugs and greater use of statins.[16] Though the above-mentioned studies indicate that more patients are currently being treated for lipid reduction than ever before, they also indicate that there remains a substantial degree of undertreatment, demonstrated by the low number of patients attaining recommended cholesterol goals. In addition, a number of studies conducted in both the primary care and specialty settings (cardiologist) in the US and Europe show that patients initiated on lipid-lowering therapies seldom reach guideline-specified goals.[17-24] In Spain, the PRECIAR 1 study, an epidemiological study involving 19 692 MI patients in primary care showed only 4.7% of the patients had LDL-C <100 mg/dL.[25] However, most of the published studies in Spain evaluating goal attainment with lipid-lowering drugs are cross-sectional in nature and at most have 3 months of follow-up. In order to better understand goal attainment with lipid-lowering drugs, a longitudinal study is needed to determine treatment patterns (e.g. titration, switching, persistency, etc.) and the effect of patient- and physician-related factors on goal attainment. A key goal of this study was to describe and compare, under usual clinical practice (i.e. 'real life'), the treatment outcomes of

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Ruiz_001-12.qxd 10/13/04 10:22 AM Page 3

goal attainment in patients who are prescribed lipid-lowering medications. Thus the objectives of this study were (i) to assess initial and subsequent lipid-lowering therapy commonly prescribed over an extended period in clinical practice, (ii) to estimate the proportion of patients switching and titrating treatment and (iii) to determine the percentage of patients attaining guideline recommended goals in different CHD risk groups. In addition, this study explored factors associated with goal attainment, including initial statin and dose, titration, length of treatment, patient characteristics and risk factors, and medical practice setting (i.e. primary care vs specialist lipid care).

Methods

Study Design and Patient Selection

Goal attainment was defined as LDL-C <100 mg/dL for CHD and CHD equivalent patients and LDL-C <130 mg/dL for non-CHD patients with two or more CHD risk factors, based on the recent international guidelines.[10,11]

This was a multicentre cohort observational study that included retrospective review of patients' medical records from 23 primary care centres and 16 lipid treatment centres across Spain. Approximately 60% of the patients were intended to be recruited at primary care centres and 40% at lipid treatment centres to replicate the distribution of hyperlipidaemia patient management practice in Spain (IMS market research data).

Physicians at the selected centres identified consecutive patients who started on lipid-lowering medications between 1 January 1998 and 30 April 1999. This 16-month period was considered the 'study index period'. The index date for each patient was the date of the first prescription for lipid-lowering drug during the study index period. To be eligible for the study, patients were required to be newly initiated on lipid-lowering therapy (i.e. no lipid-lowering prescription within 6 months prior to the index date). Patients were also required to have a physician diagnosis of angina, MI, stroke, diabetes mellitus, peripheral arterial disease, carotid artery disease, or abdominal aortic aneurysm (classified in this study as CHD and CHD equivalent patients, following the ATP III classification), or any two Framingham risk factors (smoker, physician diagnosed hypertension [≥140/90mm Hg], low high-density lipoprotein [<40 mg/dL], family history of premature coronary heart disease, and age [males ≥45 years, females ≥55 years]), classified as patients with two or more risk factors.[26] Patients also had to be aged between 18 and 75 years in 1998, have an active clinical record at the participating site for at least 3 years after the index date, have at least one lipid measure during the baseline and during the follow-up period and have no hepatic problems in the 6 months following initiation of lipid-lowering therapy (this could either be drug or non-drug induced, resulting in potential discontinuation of lipid-lowering therapy and hence lower estimates of cholesterol goal attainment).

For all patients, data for the study were collected from the following two time periods (figure 1):

- Six months prior to the index date (baseline period). This period was used to ascertain that the patient was new to lipid-lowering therapy. In addition, during this period, data on baseline demographics, comorbidities based on ICD-9 (hypertension, renal disease, mental disease, and neoplastic disease), risk factors, and cholesterol measurements prior to lipid-lowering drug initiation were collected.
- At least 3 years following the index date (study period). In this period, data on lipid-lowering treatment patterns, cholesterol measurements, and CHD events were obtained.

Data Analysis

Patient lipid-lowering drug treatment patterns were traced for the entire study period. Patients were considered to be on continuous therapy unless there was a stop date or a change in therapy date indicated in their record. Duration of patient follow-up was the number of days from the index date to the last date of record. The duration of lipid-lowering therapy was calculated as the

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Ruiz_001-12.qxd 10/13/04 10:22 AM Page 4

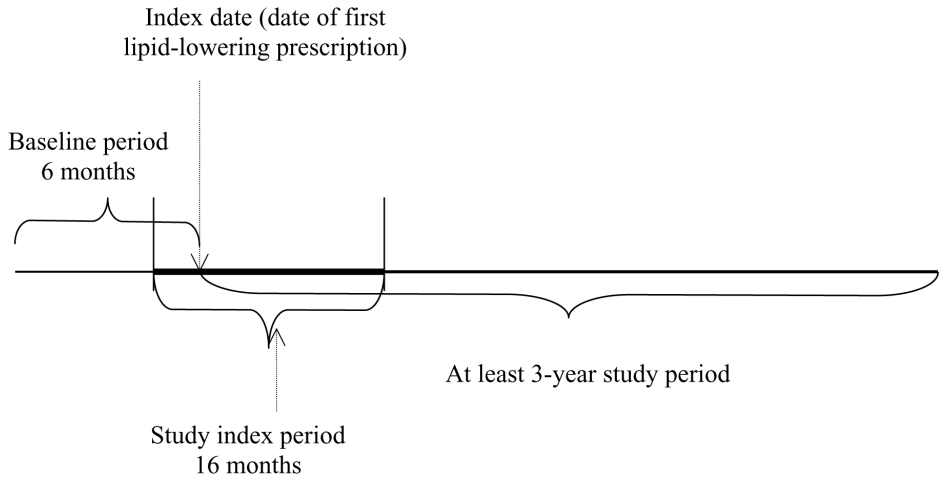

Fig. 1. Study timeline.

number of days from the first prescription of a lipid-lowering drug to the date of the last prescription plus 30 days. Since the same milligram doses of different statins are not equivalent in lipid-lowering efficacy, a statin equipotency classification based on Maron et al.[27] (table I) was used to compare the efficacy of lipid-lowering medications. Non-statins were defined as having an equipotent dose level of zero. Changing of statin therapy to a drug with a higher or lower equipotent dose level was defined as up-titration or down-titration, respectively. The magnitude of change was also measured; for instance, when a patient changed from fluvastatin 20mg (equipotent dose = 1) to atorvastatin 20mg (equipotent dose = 4) the magnitude was coded as +3. Similarly, when the switch was from atorvastatin 20mg (equipotent dose = 4) to simvastatin 10mg (equipotent dose = 2) the magnitude was coded as −2.

Baseline LDL-C and total cholesterol were based on the mean lab values within 6 months prior to the start date for initial lipid-lowering drug. Baseline cholesterol values were categorised for LDL-C into <100 mg/dL, ≥100 mg/dL and <130 mg/dL, ≥130 mg/dL and <160 mg/dL, ≥160 mg/dL and <190 mg/dL, and ≥190 mg/dL. For total cholesterol these categories were <193 mg/dL, ≥193 mg/dL and <232 mg/dL, ≥232 mg/dL and <270 mg/dL, ≥270 mg/dL and <309 mg/dL, and ≥309 mg/dL (based on quartiles).

To assess goal attainment over time, the percentage of patients attaining treatment goal was determined at 3-month time intervals for a period of 3 years (i.e. 3, 6, 9 months, etc. to a maximum of 36 months) or until the date of last record (if less than 3 years of follow-up). If the measurement was absent in a given time period, the cholesterol level value was derived from the last known measure-

Table I: Dosages (mg) of individual statins, stratified by efficacy (reproduced from Maron et al.[27])

Equipotent dose level	Atorvastatin	Simvastatin	Pravastatin	Fluvastatin	Cerivastatin	Lovastatin
0 (non-statins)	–	–	–	–	–	–
1 (very low)	–	–	10	20	0.1	10
2 (low)	5	10	20	40	0.2	20
3 (medium)	10	20	40	80	0.4	40
4 (high)	20	40	80	–	–	–
5 (higher)	40	80	–	–	–	–
6 (highest)	80	–	–	–	–	–

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Ruiz_001-12.qxd 10/13/04 10:22 AM Page 5

ment. The percentage of goal attainment was calculated for the different equipotent dose levels of statins. Additionally, the effect of change of statin potency on goal attainment was studied. The association between different factors studied (equipotent dose of statin at baseline, magnitude of change, baseline cholesterol level, age, sex, number of comorbid conditions at baseline) and goal attainment were evaluated using logistic regression. T-test and chi-square statistics were used to compare patients in the CHD/CHD equivalent group and the group with two or more risk factors. Similar analyses were conducted to compare different treatment settings (i.e. primary care centres and lipid treatment centres).

Results

Patient Demographics during Baseline Period

A total of 619 patients (45.5% CHD/CHD equivalent group and 54.5% 2+ risk factor group) were included in the study. 419 (67.6%) were from primary care centres and 200 (32.4%) were from outpatient lipid centres. The average age of the

Table II: Overall patient characteristics at baseline and by treatment site and CHD risk category

Variable		Treatment centres		CHD risk levels	
	Overall [no. (%);[a] 619]	primary care centres [no. (%);[a] 419 (67.7)]	lipid treatment centres [no. (%);[a] 200 (32.3)]	CHD/CHD equivalent [no. (%);[a] 282 (45.5)]	2+ risk factors factors [no. (%);[a] 337 (54.5)]
Sex (female)* †	296 (47.8)	223 (53.2)	73 (36.5)	111 (39.4)	185 (54.9)
Age (mean [SD]) (y)* †	60.1 (10.2)	62.1 (8.8)	55.8 (11.6)	61.2 (9.7)	59.1 (10.5)
Primary care centre*	419 (67.7)	–	–	166 (58.9)	253 (75.1)
Received exercise counselling	532 (85.9)	360 (85.9)	172 (86.0)	248 (87.9)	284 (84.3)
Received diet counselling	595 (96.1)	407 (97.1)	188 (94.0)	272 (96.4)	323 (95.8)
Cohort					
1998 index date	444 (71.7)	304 (72.6)	140 (70.0)	201(71.3)	243 (72.1)
1999 index date	175(28.3)	115 (27.4)	60 (30.0)	81 (28.7)	94 (27.9)
Smoker	282 (45.6)	173 (41.3)	109 (54.5)	132 (46.8)	150 (44.5)
Family history*	126 (20.4)	65 (15.5)	61 (30.5)	68 (24.1)	58 (17.2)
Elevated risk by age (male >45y; female >55y) †	527 (85.1)	379 (90.4)	148 (74.0)	252 (89.7)	275 (81.6)
CHD patient (angina, MI) †	118 (19.1)	62 (14.8)	56 (28.0)	118 (41.8)	0
Non-coronary atherosclerosis (CAD, PAD, AAA) †	69 (11.2)	25 (6.0)	44 (22.0)	69 (24.5)	0
Hypertension†	397 (64.1)	300 (71.6)	97 (48.5)	172 (61.0)	225 (66.8)
Peripheral vascular disease†	30 (4.8)	12 (2.9)	18 (9.0)	23 (8.2)	7 (2.1)
Diabetes mellitus	164 (26.5)	107 (25.5)	57 (28.5)	164 (58.1)	0
LDL-C categories*					
<100 mg/dL	16 (2.6)	7 (1.7)	9 (4.5)	9 (3.2)	7 (2.1)
≥100 mg/dL to <130 mg/dL	21 (3.4)	11 (2.6)	10 (5.0)	11 (3.9)	10 (3.0)
≥130 m/dL to <160 mg/dL	111 (17.9)	68 (16.2)	43 (21.5)	68 (24.1)	43 (12.7)
≥160 mg/dL to <190 mg/dL	169 (27.3)	122 (29.1)	47 (23.5)	91 (32.3)	78 (23.1)
≥190 mg/dL	282 (45.6)	207 (49.4)	75 (37.5)	94 (33.3)	188 (55.8)
Total cholesterol categories*					
<193 mg/dL	14 (2.7)	5 (1.2)	9 (4.5)	13 (4.6)	1 (0.3)
≥193 mg/dL to <232 mg/dL	88 (14.2)	60 (14.3)	28 (14.0)	61 (21.6)	27 (8.0)
≥232 mg/dL to <270 mg/dL	205 (33.1)	135 (32.2)	70 (35.0)	98 (34.6)	107 (31.7)
≥270 mg/dL to <309 mg/dL	229 (37.0)	179 (42.7)	50 (25.0)	85 (30.1)	144 (42.7)
≥309 mg/dL	83 (13.4)	40 (9.6)	43 (21.5)	25 (8.9)	58 (17.2)

a No. (%) unless otherwise indicated.

AAA = abdominal aortic aneurysm; **CAD** = carotid artery disease; **LDL-C** = low-density lipoprotein cholesterol; **MI** = myocardial infarction; **PAD** = peripheral artery disease; * $p < 0.05$ CHD/CHD equivalent vs 2+ risk factors; † $p < 0.05$ primary care vs outpatient lipid centres.

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Ruiz_001-12.qxd 10/13/04 10:22 AM Page 6

study population was 60.1 (SD 10.2) years and 47.8% were female (table II); the average follow-up time was 1332 (SD 226) days or 3.6 years, and on average participants had 22.2 (SD 16.2) follow-up visits to a GP over the study period. Significantly more CHD/CHD equivalent patients were older and male compared with 2+ risk factor patients ($p < 0.05$). The 2+ risk factor group had significantly more patients in the high baseline total cholesterol group (≥270 mg/dL) and high baseline LDL group (>190 mg/dL). In addition, differences in patient demographics were seen between patients managed at lipid treatment centres compared with patients at primary care centres (table II).

Treatment Patterns

Statins were the most common lipid-lowering medication prescribed as the initial lipid-lowering drug (90.4%), followed by fibrates (8.9%) and resins (<1%). Statins in combination with fibrates were prescribed in <1% of patients. Among statins, atorvastatin 10mg (25.7%) and simvastatin 10mg (11.8%) were the most commonly prescribed statins. There was no significant difference in initial lipid-lowering medication prescribed at primary care centres and lipid treatment centres. Fibrates and higher-dose statins were more frequently prescribed at outpatient lipid centres but this difference was not statistically significant (table III).

Patients were mainly (73.2%) prescribed lipid-lowering therapy with low (simvastatin 10mg or atorvastatin 5mg or equipotent) and medium (simvastatin 20mg or atorvastatin 10mg or equipotent) equipotent dose levels. More patients in the CHD/CHD equivalent group were prescribed statins with medium equipotent dose level compared with the 2+ risk factor group (41.5% vs 31.2%). About 45% of patients prescribed medium equipotent dose level statins had baseline LDL-C ≥190 mg/dL. Only 2.1% of patients were started with statins with high equipotent dose level (simvastatin 40mg or higher) [table IV].

A majority (57.5%) of patients had at least one change in equipotent dose levels during the study period and about 38% of the patients had an up-

Table III: Distribution of initial lipid-lowering drugs prescribed

Therapy	Overall [no. (%); 619]	Treatment centres		CHD risk levels	
		primary care centres [no. (%); 419]	lipid treatment centres [no. (%); 200]	CHD/CHD equivalent [no. (%); 282]	2+ risk factors factors [no. (%); 337]
Statins (mg)					
atorvastatin 5	1 (0.16)	1 (0.24)	–	1 (0.35)	–
atorvastatin 10	159 (25.68)	100 (23.87)	59 (29.50)	81 (28.72)	78 (23.15)
atorvastatin 20	9 (1.45)	3 (0.72)	6 (3.00)	7 (2.48)	2 (0.59)
cerivastatin 0.1	4 (0.65)	1 (0.24)	3 (1.50)	3 (1.06)	1 (0.30)
cerivastatin 0.2	36 (5.82)	25 (5.97)	11 (5.50)	12 (4.26)	24 (7.12)
fluvastatin 20	28 (4.52)	25 (5.97)	3 (1.50)	8 (2.84)	20 (5.93)
fluvastatin 40	6 (0.97)	3 (0.72)	3 (1.50)	2 (0.71)	4 (1.19)
lovastatin 10	36 (5.82)	33 (7.88)	3 (1.50)	8 (2.84)	28 (8.31)
lovastatin 20	65 (10.50)	55 (13.13)	10 (5.00)	34 (12.06)	31 (9.20)
lovastatin 40	2 (0.32)	2 (0.48)	–	–	2 (0.59)
pravastatin 10	26 (4.20)	19 (4.53)	7 (3.50)	11 (3.90)	15 (4.45)
pravastatin 20	49 (7.91)	28 (6.68)	21 (10.50)	23 (8.15)	26 (7.71)
pravastatin 40	2(0.32)	–	2 (1.00)	1 (0.35)	1 (0.30)
simvastatin 10	73 (11.79)	55 (13.13)	18 (9.00)	32 (11.35)	41 (12.17)
simvastatin 20	58 (9.37)	39 (9.31)	19 (9.50)	35 (12.41)	23 (6.82)
simvastatin 40	4 (0.64)	1 (0.24)	3 (1.50)	1 (0.35)	3 (0.89)
Fibrates	55 (8.88)	27 (6.44)	28 (14.0)	23 (8.15)	32 (9.49)
Resins	4 (0.64)	2 (0.48)	2 (1.00)	–	4 (0.64)
Combinations (statin + fibrates)	2 (0.32)	–	2 (1.00)	–	2 (0.32)

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Ruiz_001-12.qxd 10/13/04 10:22 AM Page 7

Table IV: Potency of initial lipid-lowering drugs prescribed

Potency[a]	All patients [no. (%)]	CHD/CHD equivalent patients [no. (%)]	2+ risk factor patients [no. (%)]
0 (fibrates or resins)	59 (9.53)	23 (8.16)	36 (10.68)
1 (very low potency)	94 (15.19)	30 (10.64)	64 (18.99)
2 (low potency)	231 (37.32)	104 (36.88)	127 (37.69)
3 (medium potency)	222 (35.86)	117 (41.49)	105 (31.16)
4 (high potency)	13 (2.10)	8 (2.84)	5 (1.48)
5 > (very high potency)	0	0	0

a Potency numbers: 0 = fibrates and resins; 1 = pravastatin 10mg or equipotent; 2 = simvastatin 10mg or equipotent; 3 = simvastatin 20mg or equipotent; 4 = simvastatin 40mg or equipotent; 5 = simvastatin 80mg or equipotent.

Table V: Distribution of cholesterol lab measures by different time periods after initiation on lipid-lowering therapy

Time period (months after initiation)	No. of patients with cholesterol measures	Average (SD) no. of cholesterol measures
0–3	118	1.02 (0.13)
3–6	278	1.04 (0.22)
6–9	213	1.03 (0.13)
9–12	277	1.03 (0.18)
12–15	216	1.02 (0.15)
15–18	224	1.02 (0.13)
18–21	204	1.02 (0.15)
21–24	218	1.04 (0.20)
24–27	206	1.03 (0.18)
27–30	197	1.04 (0.19)
30–33	203	1.03 (0.17)
33–36	196	1.04 (0.19)

titration. The number of changes of lipid-lowering therapies was similar in both the CHD/CHD equivalent group and the 2+ risk factor group. A higher proportion of patients who were initiated on fibrates or statins with very low equipotent dose level had a change of potency (69.5% and 72.3%) compared with patients started on statins with low or medium equipotent dose levels (51.1% and 54.9%). This trend was seen in both CHD/CHD equivalent and 2+ risk factor patients. Patients started on statins with medium and high equipotent dose levels experienced the highest proportion of down-titration (39.6% and 46.1%, respectively). The magnitude of switch was mostly one equipotent dose (+1 or −1).

Goal Attainment and Factors Affecting Goal Attainment

The average number of cholesterol lab measures during the study period was 4.4 (SD 2.2); the numbers of patients with cholesterol measures were similar in the different time periods after initiation of lipid-lowering therapy, and patients who had cholesterol tests on average had one test in a 3-month period (table V). The average LDL-C reduction required at baseline to attain goal was 39.09% for the CHD/CHD equivalent group and 28.86% for the 2+ risk factor group. LDL-C levels decreased within the 3 months after treatment start and stabilised around the obtained lower cholesterol levels (figure 2). The average observed reduction in LDL-C values was 26% for the CHD/CHD equivalent group and 22% for the 2+ risk group at the end of the follow-up. At the end of the study period, 20.2% of all CHD/CHD equivalent patients and 31.4% of 2+ risk factor group patients were at their cholesterol goal levels or lower. Overall, only 12.9% of all patients achieved goal on their initial statin; of the patients who did not reach goal on their initial therapy, 66.0% had a change in potency of their treatment, and only 23.4% of these patients reached goal (figure 3). Of the patients not at goal, 28.7% required additional LDL-C reductions greater than 30%, and 35.6% required LDL-C reductions between 15% and 30% to attain the recommended cholesterol goals.

A logistic regression model for goal attainment controlling for age, sex, baseline comorbidities, statin potencies, potency change, baseline cholesterol levels and CHD, found that older patients were more likely to attain goal (OR 1.02; 95% CI 1.01, 1.05). CHD/CHD equivalent patients were less likely to reach goal than 2+ risk factor patients (OR 0.47; 95% CI 0.31, 0.72) and patients

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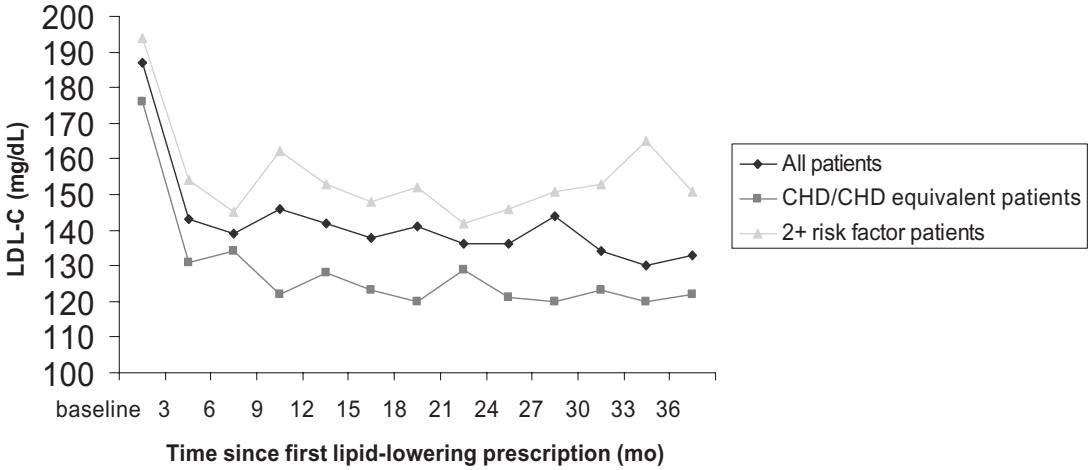

Fig. 2. Average cholesterol values before and after initiation of lipid therapy.

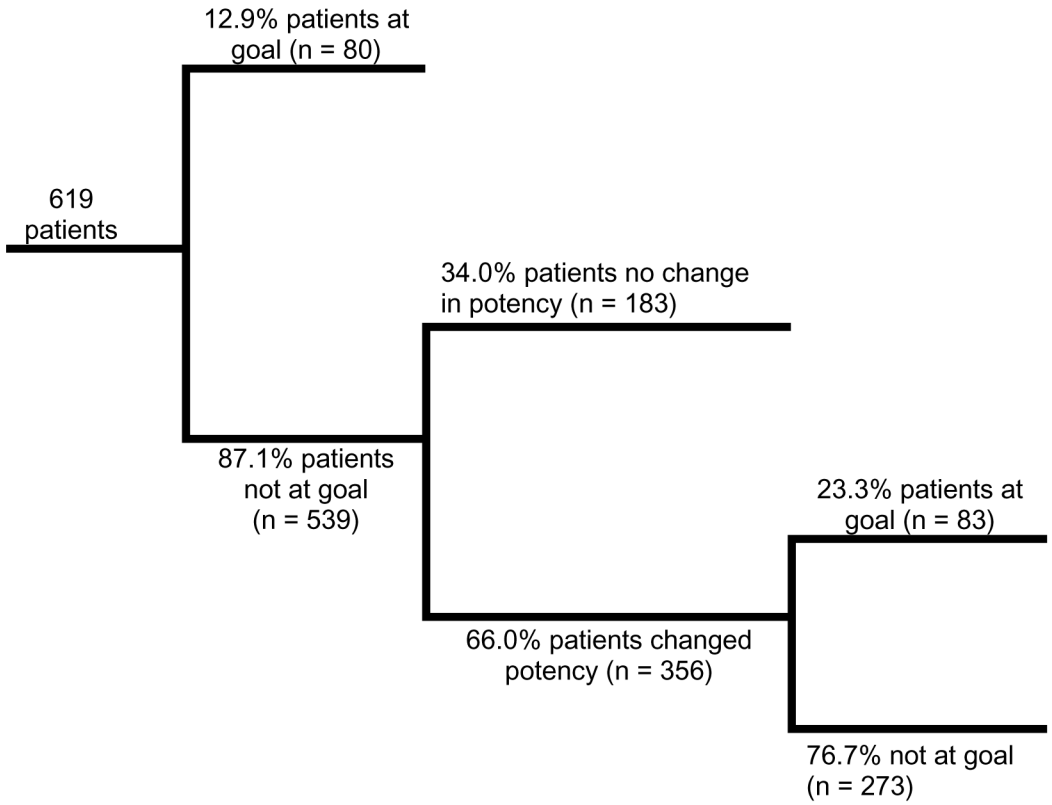

Fig. 3. Overall goal attainment and lipid management.

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Ruiz_001-12.qxd 10/13/04 10:22 AM Page 9

with high baseline LDL-C (≥190 mg/dL) were less likely to reach recommended cholesterol goal than patients with baseline LDL-C between 100 and 130 mg/dL (OR 0.53; 95% CI 0.35, 0.79).

Discussion

The quantity and quality of clinical evidence available on the benefits of hypercholesterolaemia treatment are more comprehensive than for any other medical intervention.[5,6,28] As a consequence of this growing body of evidence, the latest Global Plan for the Management of Ischemic Heart Disease for 2004-2007 issued by the Spanish Ministry of Health recommends aggressive reductions in LDL-C for both primary and secondary prevention of CHD.[12] This study, based on a retrospective chart review of patients initiated on lipid-lowering drugs, evaluated how patients are currently managed for lipid reduction and also evaluated the proportion of patients attaining the recommended cholesterol goal in Spain.

This was a cohort study with retrospective patient chart review of at least 3 years of data and hence in this regard is more representative of patients having adequate follow-up data or more persistent patients. The major advantage of such a study design is that it evaluates lipid management strategies employed by physicians in daily practice, which cannot be captured in protocol-driven randomised clinical trials, and therefore it has more relevance to the healthcare system being studied. To our knowledge, this is the only study that has used this type of design to evaluate the relationship between treatment patterns and cholesterol goal attainment in Spain. The limitation of the study design is that it is restricted to data collected in the clinical practice setting and may be influenced by the treating physician's decision to conduct the relevant lab tests and report results in the patient chart. For example, it is possible that normal lab results may not be reported in the chart. In addition, inferences about cause and effect are open to bias from confounding factors unless care is taken to stratify the patients or otherwise control for these factors. Several of the risk factors, such as diabetes and prior cardiovascular events, that may have an effect on goal attainment were included in the current analysis.

This study does provide some important findings. It confirms the other findings currently reported in the literature on cholesterol goal attainment in usual clinical practice in Spain. The ELIPSE study,[24] which assessed the level of lipid control in post-MI patients treated in primary care, showed that only 30% of the patients had an LDL-C <130 mg/dL, and only 9% had an LDL-C <100 mg/dL. Also consistent with these results, the PRECIAR 1 study,[25] conducted in primary care on secondary prevention patients, concluded that only 24.2% of the treated patients achieved LDL-C levels <130 mg/dL, and the PREVESE II study,[15] conducted in post-MI patients at hospital discharge, again found that cholesterol management in this high-risk population was deficient, with an average LDL-C of 139.6 mg/dL and only 30.5% of the patients being prescribed lipid-lowering drugs (the majority of which were statins). These studies and others such as the 3C[28] have consistently shown a very low level of attainment of cholesterol target levels in Spanish patients with a high cardiovascular risk profile. Actually, this situation is not unique to Spain, but is a general problem throughout Europe, as demonstrated by the EUROASPIRE I and II studies.[16] In this study, we go a step further in trying to understand the reasons for the low goal attainment rates by adding a very valuable longitudinal perspective on the pattern of hyperlipidaemia management. This study demonstrated that only 13% of patients attained LDL-C goal on initial prescribed lipid therapy, and an additional 13% attained LDL-C goal after a change in initial therapy. The main contribution of this study is providing evidence that even after an extended follow-up (average of 3.6 years) after starting treatment, there is a low likelihood that a high-risk patient will attain the recommended LDL-C level.

In addition, owing to the longitudinal nature of this study, it can be clearly demonstrated that patients in Spain are mostly initiated on low-dose statins and the majority of patients not at goal had some type of intervention in terms of switches or up- or down-titration seen in current clinical practice in

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Ruiz_001-12.qxd 10/13/04 10:22 AM Page 10

Spain. This finding is unique to Spain, as there are no other reports in the literature of such a high intervention rate, and this may be reflective of the study setting, as we had about 32% of patients recruited from progressive outpatient lipid treatment centres. However, in spite of this high intervention rate, the overall goal attainment rate in these patients was still quite low. The REVERSAL study[30] demonstrated that aggressive lipid reduction in CHD patients could substantially reduce coronary artery atheroma burden and progression. Additionally, the recent findings of the PROVE IT study[13] demonstrated that reducing cholesterol levels to as low as 62 mg/dL substantially reduced mortality. Therefore, our current finding that CHD patients and patients with high baseline cholesterol (i.e. the patients who stand to gain most from aggressive lipid control) were least likely to attain even the recommended cholesterol goal with current lipid-lowering therapies is noteworthy.[13,29]

Although this current study does not provide specific insights into the reasons for patient and physician beliefs that might be important factors leading to the gap between guidelines that recommend aggressive lipid control and actual practice, it does provide important information on current lipid-lowering drug therapy and its effectiveness in clinical practice. The results of the study clearly show there is need for more effective management of hypercholesterolaemia patients. Based on data from clinical trials, each doubling of statin dose provides on average 7% reduction in LDL-C.[31] However, statin titration is not routinely done in clinical practice; in the current study we had a relatively high number (38%) of patients who were up-titrated and only 20% of these patients attained goal. Thus, statin-alone therapy that focuses on one of the two main sources of cholesterol might not address the current unmet need of lipid-lowering therapy. While combinations of statins with other classes of lipid-lowering drugs, such as fibrates, resins and niacin, are effective, they have not been widely used because of poor safety/tolerability or inconvenience (<1% of the patients in our study received combination therapy with statins). A recent trial has shown that, CHD patients or multiple cardiovascular risk patients not at cholesterol goal with statin alone therapy benefit from coadministration of ezetimibe (a cholesterol absorption inhibitor) with 25% incremental LDL-C reduction, resulting in a 72% goal attainment in ezetimibe arm versus 19% goal attainment in the statin arm.[32] Therapy of ezetimibe coadministered with a statin, which acts by inhibiting both cholesterol absorption and synthesis, might help more patients attain guideline-recommended cholesterol levels in clinical practice, especially for patients at high risk of cardiovascular events who would benefit the most from aggressive lipid reduction.

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Ruiz_001-12.qxd 10/13/04 10:22 AM Page 11

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Ruiz_001-12.qxd 10/13/04 10:22 AM Page 12

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