

OBSERVATIONAL AND RETROSPECTIVE STUDY TO ANALYZE THE CHANGES IN LIPID AND GLYCEMIC PROFILES IN PATIENTS WITH METABOLIC SYNDROME AFTER TREATMENT WITH STATINS: ESMET STUDY



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Introduction

- Evidence suggests that the diabetogenic risk associated with statins can rise in patients with pre-existing risk factors such as those with metabolic syndrome (MS).

This risk depends on the statin dose and patient population

Objective

- To assess changes in lipid and glycemic profile in dyslipidemic subjects with MS after statin therapy.

Methods

- Observational, retrospective, multi-center study, conducted in 40 endocrinology Spanish hospitals.
- Each endocrinologist included the first 10 patients >18 years with MS, HDL-C<40 mg/dl in men and <50 mg/dl in women and 2 or more MS risk factors according to NCEP-ATP III criteria, treated with statins for at least 12 weeks before their inclusion, and had signed informed consent.
- Demographic variables, medical history, diabetic complications, anthropometric data and analytical and therapeutic profiles were collected before and after starting statin therapy.
- ADA objectives for lipid and glycemic control, student *t* test for paired data or the Wilcoxon sign tests for quantitative variables, and McNemar test or Fisher's exact test for qualitative variables were used. A *p*<0.05 was significant.

Results

- The baseline characteristics of the 345 patients evaluated in the population studied with MS are shown in Table 1.
- After statin therapy, there was a decrease in total cholesterol, triglycerides (TGs), LDL-C, HbA1c and fasting glucose (FG), and an increase in HDL-C (*p*<0.0001 for all) (Table 2), and in the percentage of patients achieving the ADA objectives (*p*<0.0001 for all) (Table 4).
- These changes were similar with all statins (Table 3)
- Multivariate analysis showed a greater increase of HDL-C with pitavastatin 18,4% (vs atorvastatin 7.4%; *p*=0.0094, and vs simvastatin 9.6%; *p*<0.0001) (Table 3). In univariate analysis a reduction on the percentage of change on FG (4.8 ± 20.5%; *p*<0.0161) after treatment with pitavastatin was observed (Table 3)

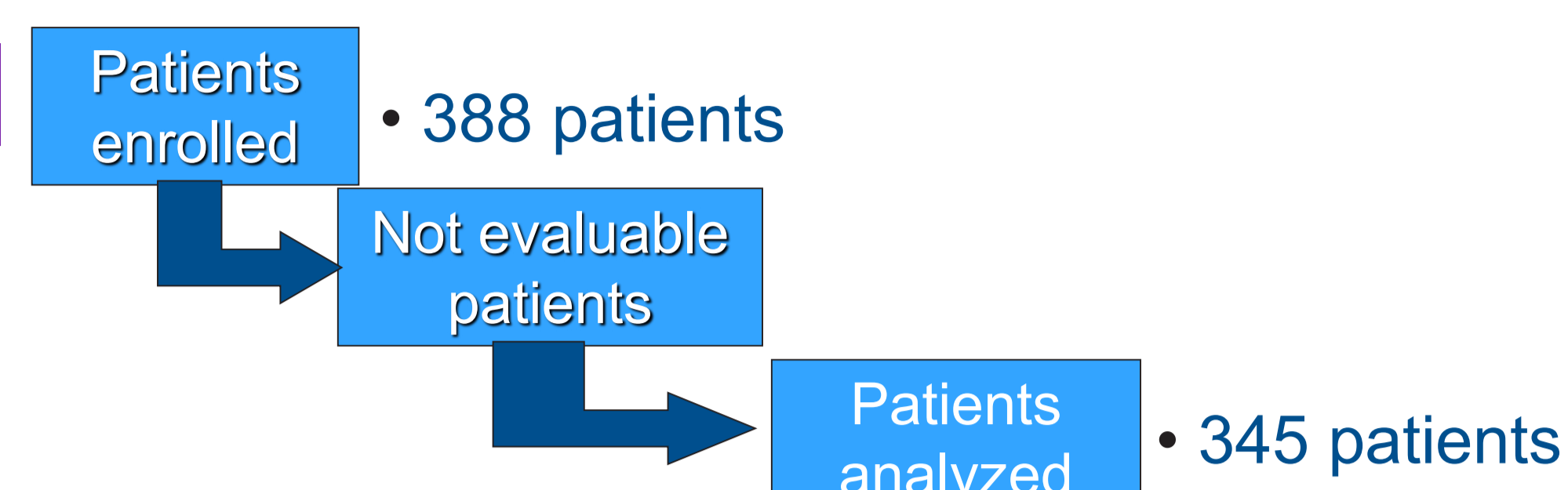


Figure 1. Patients included in the study

Table 1. Baseline characteristics of the studied population with metabolic syndrome

CHARACTERISTICS	N=345
SOCIO-DEMOGRAPHIC DATA	
Sex (M/F)	186 / 159
Age (years)	60.9 ± 9.3
Diagnosis of metabolic syndrome (years)	6.1 ± 5.9
PHYSICAL EXAMINATION	
Weight (Kg.)	88.7 ± 15.1
Body mass index (Kg/m ²)	32.4 ± 4.7
Waist circumference (WC)	107.9 ± 11.1
Systolic blood pressure (mmHg)	139.3 ± 15.2
Diastolic blood pressure (mmHg)	83.9 ± 10.1
CARDIOVASCULAR RISK FACTORS	
Smoking / Non smoking (%)	37 (10.9) / 100 (29.5)
Alcohol consumption (%)	91 (27.3)
Type 1 / type 2 Diabetes Mellitus(%)	10 (2.9) / 269 (78)
Hypertension (%)	279 (80.9)
Dyslipidemia (%)	345 (100)
Family history of coronary artery disease (%)	56 (16.2)
MEDICAL HISTORY OF MACRO AND MICROVASCULAR DISEASE	
Cardiovascular disease (%)	65 (18.8)
Cerebrovascular disease (%)	6 (1.7)
Renal disease (%)	31 (9)
Peripheral vascular disease (%)	21 (6.1)
Microvascular disease (%)	44 (12.8)
CRITERIA FOR METABOLIC SYNDROME (NCEP-ATP III)	
HDL-C < 40 mg/dl in M or HDL-C < 50 mg/dl in F (%)	345 (100)
Abdominal obesity (WC > 102 in M and >82 cm in F)(%)	310 (89.9)
Blood pressure ≥ 130/85 mmHg (%)	268 (77.7)
Fasting glucose ≥ 110 mg/dl (%)	305 (88.4)
Triglycerides ≥ 150 mg/dl	268 (77.7)
LIPID-LOWERING THERAPY	
Pitavastatin (%)	164 (47.5)
Atorvastatin (%)	72 (20.9)
Simvastatin (%)	59 (17.1)
Rosuvastatin (%)	42 (12.2)
Other (Pravastatin, Lovastatin) (%)	8 (2.3)
ANTI-DIABETIC THERAPY	
Lifestyle changes (%)	209 (66.6)
Metformin (%)	232 (67.2)
Insulin (%)	89 (25.8)
DPP-4 inhibitors (%)	87 (25.2)
GLP-1 analogs (%)	68 (19.7)
Glinides (%)	35 (10.1)
Sulfonylureas (%)	31 (9)
Other (Pioglitazon, SGLT-2 inhibitors, alfa glucosidase inhibitors) (%)	16 (4.6)
ANTI-HYPERTENSIVE THERAPY	
ARB II (%)	174 (50.4)
Diuretics (%)	120 (34.8)
ACEIs (%)	89 (25.8)
Calcium channel blockers (%)	67 (19.4)
Beta-blockers (%)	45 (13)
Alfa-blockers (%)	6 (1.7)
OTHER THERAPIES	
Antiplatelet / Anticoagulants (%)	142 (41.2)
Antiobesity (%)	10 (2.9)

Table 2. Change in glycemic and lipid profile and cardiovascular risk according to Framingham calibrated for Spain (REGICOR) in the studied population with metabolic syndrome. CVR= Cardiovascular risk

	Basal	Current	Change	p	Change (%)	P
HbA1c (%)	7.1 ± 1.1	6.9 ± 1.2	-0.2 ± 0.8	0.1615	-2.3 ± 10.8	0.0118
FG (mg/dl)	144.7 ± 51.2	129.9 ± 42.2	-14.8 ± 45.7	<0.0001	-5.8 ± 24.5	<0.0001
Cholesterol(mg/dl)	221.1 ± 44.8	176.7 ± 37.0	-44.4 ± 43.0	<0.0001	-18.3 ± 17.0	<0.0001
TGs (mg/dl)	203.3 ± 218.4	163.3 ± 149.7	-39.9 ± 109.2	<0.0001	-16.2 ± 33.1	<0.0001
LDL-C (mg/dl)	143.8 ± 43.1	100.3 ± 31.4	-43.6 ± 39.6	<0.0001	-25.9 ± 27.6	<0.0001
HDL-C (mg/dl)	37.5 ± 5.7	43.4 ± 10.4	+5.9 ± 9.1	<0.0001	+16.5 ± 25.6	<0.0001
CVR (%)	8.4 ± 5.2	5.7 ± 3.3	-2.7 ± 3.8	<0.0001		
CVR <10 (%)	256 (74.2)	311 (90.1)		<0.0001		
CVR 10-20 (%)	78 (22.6)	34 (9.9%)		<0.0001		
CVR >20 (%)	11 (3.2)	0 (0)		<0.0001		

Table 3. Changes in glycemic and lipid parameters, and multivariate analysis of the percentage change in them by type of statin monotherapy, in the studied population with metabolic syndrome

	Basal	Current	Change	p	Change (%)	p
HbA1c						
Atorvastatin	7.2 ± 1.2	7.0 ± 1.0	-0.2 ± 0.6	0.1195	-2.0 ± 8.5	0.2064
Pitavastatin	7.0 ± 0.9	6.9 ± 1.0	-0.1 ± 0.5	0.1315	-1.7 ± 7.5	0.1520
Rosuvastatin	7.4 ± 1.1	6.8 ± 1.0	-0.7 ± 0.7	0.0394	-8.7 ± 8.5	0.0354
Simvastatin	7.1 ± 0.9	6.8 ± 1.1	-0.4 ± 1.0	0.0519	-4.9 ± 14.9	0.0890
FG (mg/dl)						
Atorvastatin	154.5 ± 52.0	137.3 ± 36.3	-17.2 ± 47.8	0.0129	-5.5 ± 25.3	0.1272
Pitavastatin	134.6 ± 43.6	123.8 ± 35.9	-10.8 ± 34.9	0.0017	-4.8 ± 20.5	0.0161
Rosuvastatin	145.2 ± 35.8	131.6 ± 33.2	-13.6 ± 33.1	0.0508	-6.6 ± 20.6	0.1204
Simvastatin	139.7 ± 35.9	134.5 ± 52.2	-5.2 ± 47.1	0.4699	-2.1 ± 29.0	0.6391
LDL-C (mg/dl)						
Atorvastatin	128.6 ± 37.6	91.9 ± 28.3	-36.7 ± 31.6	<0.0001	-25.9 ± 20.6	<0.0001
Pitavastatin	144.9 ± 40.0	104.1 ± 27.8	-40.8 ± 34.0	<0.0001	-25.1 ± 20.1	<0.0001
Rosuvastatin	155.4 ± 38.7	96.7 ± 26.9	-58.7 ± 36.2	<0.0001	-35.7 ± 19.4	<0.0001
Simvastatin	139.4 ± 33.5	97.7 ± 29.7	-41.7 ± 32.4	<0.0001	-28.2 ± 21.0	<0.0001
HDL-C (mg/dl)						
Atorvastatin	38.3 ± 5.7	41.0 ± 9.3	+2.7 ± 7.6	0.0154	+7.4 ± 19.7	0.0097
Pitavastatin	37.7 ± 5.8	44.3 ± 9.5	+6.6 ± 8.2	<0.0001	+18.4 ± 23.4	<0.0001
Rosuvastatin	35.8 ± 4.5	39.1 ± 8.6	+3.3 ± 8.6	0.0656	+10.3 ± 26.6	0.0633
Simvastatin	40.2 ± 6.2	44.3 ± 11.3	+4.1 ± 7.9	0.0017	+9.6 ± 19.2	0.0022
TGs (mg/dl)						
Atorvastatin	189.9 ± 126.9	148.2 ± 71.7	-41.8 ± 80.5	0.0005	-14.8 ± 26.9	0.0003
Pitavastatin	176.6 ± 89.1	140.8 ± 44.5	-35.8 ± 68.4	<0.0001	-14.2 ± 23.3	<0.0001
Rosuvastatin	181.6 ± 60.1	152.4 ± 48.1	-29.2 ± 50.9	0.0086	-12.0 ± 31.6	0.0687
Simvastatin	160.3 ± 66.1	132.3 ± 57.8	-27.9 ± 50.6	0.0008	-14.0 ± 29.7	0.0034
Multivariate analysis of the change in HbA1c						
Atorvastatin		0.6096			0.6096	0.5502
Pitavastatin		0.5502			0.2373	0.2373
Simvastatin						0.5502
Multivariate analysis of the change in fasting glucose						
Atorvastatin		0.7546			0.5794	0.8864
Pitavastatin		0.7546			0.7019	0.6139
Rosuvastatin		0.5794			0.7019	0.4893
Simvastatin		0.8864			0.6139	0.4893
Multivariate analysis of the change in HDL-C						
Atorvastatin		0.0074			0.0009	0.6823
Pitavastatin		0.0074			0.1407	0.0445
Rosuvastatin		0.0009			0.1407	0.0060
Simvastatin		0.6823			0.0445	0.0060
Multivariate analysis of the change in LDL-C						
Atorvastatin		0.1455			0.0059	0.0123
Pitavastatin		0.1455			0.0556	0.1069
Rosuvastatin		0.0059			0.0556	0.7542
Simvastatin		0.0123			0.1069	0.7542
Multivariate analysis of the change in triglycerides						
Atorvastatin		0.9419			0.8031	0.8344
Pitavastatin		0.9419			0.8265	0.8565
Rosuvastatin		0.8031			0.8265	0.9598
Simvastatin		0.8344			0.8565	0.9598

Table 4. Changes in achieving glycemic and lipid goals according to statin monotherapy, in the studied population with metabolic syndrome

HbA1c<7%	Basal	N	Current	N	p
Atorvastatin	15 (50)	30	14 (46.7)	30	0.5637
Pitavastatin	23 (52.3)	44	23 (52.3)	44	1.0000
Rosuvastatin	3 (42.9)	7	5 (71.4)	7	0.1573
Simvastatin	12 (41.4)	29	16 (55.2)	29	0.2059
FASTING GLUCOSE< 110 mg/dl					
Atorvastatin	9 (17.6)	51	9 (17.6)	51	0.5637
Pitavastatin	31 (28.7)	108	43 (39.8)	108	0.0143
Rosuvastatin	4 (16.0)	25	7 (28.0)	25	0.1797
Simvastatin	7 (16.3)	43	19 (44.2)	43	0.0013
LDL-C<100 mg/dl					
Atorvastatin	8 (15.7)	51	32 (62.7)	51	<0.0001
Pitavastatin	12 (11.1)	108	44 (40.7)	108	<0.0001
Rosuvastatin	3 (12.0)	25	15 (60.0)	25	0.0005
Simvastatin	6 (14.0)	43	27 (62.8)	43	<0.0001
HDL-C> 40 in Male y > 50 mg/dl in Female					
Atorvastatin	0 (0)	51	16 (31.4)	51	<0.0001
Pitavastatin	0 (0)	108	49 (45.4)	108	<0.0001
Rosuvastatin	0 (0)	25	7 (28.0)	25	0.0082
Simvastatin	0 (0)	43	16 (37.2)	43	<0.0001
Triglycerides< 150 mg/dl					
Atorvastatin	21 (41.2)	51	29 (56.9)	51	0.0325
Pitavastatin	33 (30.6)	108	67 (62.0)	108	<0.0001
Rosuvastatin	7 (28.0)	25	15 (60.0)	25	0.0114
Simvastatin	18 (41.9)	43	30 (69.8)	43	0.0027

Conclusions

- In the MS patients studied, lipid and glycemic parameters and the percentage of patients achieving the ADA objectives improved after statin therapy. Pitavastatin could have better cardiovascular benefit due to the greater increase in HDL-C

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