

Comparison of the efficacy, safety and tolerability of policosanol and atorvastatin in patients with type II hypercholesterolemia

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Recibido: 12 de diciembre de 2003. Aceptado: 10 de noviembre de 2004.

Palabras clave: policosanol, atorvastatina, hipercolesterolemia tipo II, drogas reductoras de colesterol.
Key words: policosanol, atorvastatin, type II hypercholesterolemia, cholesterol-lowering drugs.

RESUMEN. La hipercolesterolemia es uno de los más importantes factores de riesgo coronario. El principal objetivo en el control de la dislipidemia es la disminución de las concentraciones elevadas de LDL - C. El policosanol es un medicamento hipocolesterolemizante purificado de la cera de la caña de azúcar con un intervalo terapéutico entre 5 y 20 mg/d, que reduce significativamente la concentración de LDL - C en el suero sanguíneo. La atorvastatina es un inhibidor de la HMGCoA reductasa, el cual a través de su intervalo terapéutico (10 a 80 mg/d) muestra un marcado efecto hipolipemiente, superior a otras estatinas hasta ahora disponibles. Este estudio se lleva a cabo para comparar la eficacia, seguridad y tolerabilidad del policosanol y la atorvastatina en pacientes con hipercolesterolemia tipo II. Este estudio se realizó en pacientes de ambos sexos de forma aleatorizada y a simple ciegas con grupos paralelos. Después de 5 semanas de dieta baja en colesterol, 175 pacientes con valores de colesterol $\geq 3,4$ mmol/L se trataron aleatoriamente con policosanol o atorvastatina (10 mg) una vez al día en horario de la cena y durante 8 semanas. Se realizó la evaluación del perfil de los lípidos del suero y de los indicadores de seguridad, así como de los eventos adversos (EA). Después de 8 semanas el policosanol (10 mg/d) disminuyó significativamente ($p < 0,000\ 001$ vs línea de base) la LDL - C (27,0 %), TC (19,6 %), LDL-C/colesterol de lipoproteína de alta densidad (HDL-C) (30,1 %) y TC/HDL-C (23,9 %), así como TG (12,4 %). ($p < 0,000\ 1$ vs valores basales). Por otra parte, la atorvastatina (10 mg/d) redujo significativamente ($p < 0,000\ 001$ vs valores basales) la LDL - C (35,2 %), TC (26,2 %), LDL-C/HDL-C (34,5 %), TC/HDL-C (25,9 %) y ($p < 0,000\ 1$) TG (10,2 %). La atorvastatina fue más efectiva que el policosanol ($p < 0,001$) para reducir la LDL-C y TC ($p < 0,000\ 1$). El policosanol, pero no la atorvastatina incrementó las HDL - C de manera significativa ($p < 0,000\ 1$) en un 10,4 %. (En el chequeo intermedio realizado a las 4 semanas, los cambios inducidos por ambos medicamentos sobre el perfil de los lípidos del suero eran ya significativos, siendo el efecto de la atorvastatina similar al obtenido a las 8 semanas, mientras que el policosanol continuó incrementando su efecto a lo largo del tratamiento. Tanto el policosanol como la simvastatina fueron bien tolerados. La atorvastatina incremento significativamente ($p < 0,01$) la CPK y la ALAT mientras que el policosanol disminuyó estos valores ($p < 0,01$) en relación a los basales, pero los individuales permanecieron dentro del intervalo normal. Seis pacientes resultaron baja del estudio debido a eventos adversos, todos del grupo de la atorvastatina. De 17 pacientes que reportaron EA durante el estudio, tres fueron del grupo policosanol y 14 del grupo atorvastatina ($p < 0,01$), que reportaron un total de 4 y 23 AE, respectivamente. La atorvastatina (10 mg/d) por 8 semanas fue más efectiva que el policosanol en igual dosis para reducir LDL-C y TC en pacientes con hipercolesterolemia tipo II, pero similarmente efectivos para reducir las concentraciones en suero de TG, LDL - C/HDL - C y CT/HDL -

C. El policosanol, pero no la atorvastatina fue efectivo en el incremento de la concentración en el suero de HDL - C. El policosanol fue mejor tolerado que la atorvastatina de acuerdo con los indicadores bioquímicos de seguridad y el reporte de EA.

ABSTRACT. Hypercholesterolemia is a major coronary risk factor. The main goal of dyslipidemia control in is to lower elevated LDL-C levels. Policosanol is a cholesterol-lowering drug purified from sugar cane wax with a therapeutic range from 5 to 20 mg/d, which significantly reduces LDL-C levels. Atorvastatin is an HMGCoA reductase inhibitor, which across its dose range (10 - 80 mg/d) shows significantly greater lipid-lowering effects than previously available statins. This study was undertaken to compare the efficacy, safety and tolerability of policosanol and atorvastatin on patients with type II hypercholesterolemia. This randomized, single-blinded, parallel-group study was conducted in patients of both sexes with type II hypercholesterolemia. After 5 weeks on cholesterol-lowering diet, 175 patients showing LDL-C values ≥ 3.4 mmol/L were randomized to policosanol or atorvastatin 10-mg tablets once daily with the evening meal for 8 weeks. Assessment of lipid profile, safety indicators and adverse events (AE) was done. After 8 weeks, policosanol 10 mg/d significantly ($p < 0.000\ 001$ vs baseline) lowered LDL-C (27.0 %), TC

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(19.6%), LDL-C/high-density lipoprotein-cholesterol (HDL-C) (30.1%) and TC/HDL-C (23.9%) ratios, as well as ($p < 0.00001$) TG (12.4%). In turn, atorvastatin 10 mg/d decreased ($p < 0.000001$ vs baseline) LDL-C (35.2%), TC (26.2%), LDL-C/HDL-C (34.5%), TC/HDL-C (25.9%) and ($p < 0.0001$) TG (10.2%). Atorvastatin was more effective than policosanol ($p < 0.001$) to reduce LDL-C and TC ($p < 0.0001$) Policosanol, but not atorvastatin, significantly increased HDL-C by 10.4% ($p < 0.0001$). At the interim check-up performed at week 4, the changes induced by both drugs on lipid profile were yet significant, the effects of atorvastatin being similar to those achieved at week 8, while policosanol increased the effects with treatment duration. Both policosanol and atorvastatin were safe and well tolerated. Atorvastatin significantly increased ($p < 0.01$) CPK and ALAT levels respect to baseline, while policosanol decreased ($p < 0.01$) such values. Policosanol, but not atorvastatin, decreased systolic pressure ($p < 0.01$) compared with baseline, but individual values remained within normal ranges. Six patients withdrew from the study due to AE, all from atorvastatin group, reported 12 AE during the study. Seventeen patients reported some AE during the study: three policosanol and 14 atorvastatin patients ($p < 0.01$) who reported a total of 4 and 23 AE, respectively. Atorvastatin (10 mg/d) for 8 weeks was more effective than similar doses of policosanol to reduce LDL-C and TC in patients with type II hypercholesterolemia, but similarly effective to reduce TG and both LDL-C/HDL-C and TC/HDL-C ratios. Policosanol, however, but not atorvastatin, was effective to increase HDL-C levels. Policosanol was better tolerated than atorvastatin as indicated blood biochemistry safety indicators and AE report.

INTRODUCTION

Coronary heart disease (CHD) is the major cause of mortality in adult population.¹ Hypercholesterolemia, mainly that associated with elevated plasma levels of low-density lipoprotein cholesterol (LDL-C) is a major risk factor for CHD,^{2,6} and endpoint clinical studies have proven, beyond any doubt, the clinical benefits of lowering LDL-C levels.⁷⁻¹³

Hence, expert guidelines recommend hypercholesterolemia management in middle-aged and elderly patients as a part of the coronary prevention strategy.^{2,3} Coexistence of hypercholesterolemia with other non-lipid risk factors increases the global coronary risk and updated coronary prevention places LDL-C goals as the cornerstone of hypercholesterolemia management, which become more restrictive for indi-

viduals at highest risk, such as those at secondary prevention, diabetics and patients with several risk factors.^{2,3}

The adherence to a step I cholesterol-lowering diet is the first-choice therapy for hypercholesterolemia management,^{2,3} but such measures alone are often not enough to reach a desirable control. Then, cholesterol-lowering drugs must be indicated to these patients, HMG-CoA reductase inhibitors (statins) being a first-choice pharmacological alternative and the most prescribed drugs worldwide for lowering elevated LDL-C levels.^{2,3}

Atorvastatin is a member of statin class that, across its dosage range (10 - 80 mg/d), induces marked reductions of plasma LDL-C, greater than those induced by simvastatin, pravastatin, lovastatin, fluvastatin and cerivastatin.¹⁴⁻²² Thus, it is a suitable reference to compare the cholesterol-lowering effects of any other hypocholesterolemic drug. Atorvastatin is generally well tolerated and most drug-related adverse events (AE) are mild and transient, gastrointestinal symptoms being the most frequent. As occurs with other statins, persistent increases on serum transaminases and creatinphosphokinase (CPK), myalgia and myopathy have been associated to atorvastatin treatment.¹⁴⁻²²

Policosanol is a mixture of higher aliphatic primary alcohols purified from sugar cane (*Saccharum officinarum*, L.) wax with cholesterol-lowering effects.²³ Policosanol lowers cholesterol by inhibiting cholesterol biosynthesis in a step between acetate consumption and mevalonate production,²⁴⁻²⁶ through an indirect regulation of HMG CoA reductase activity.²⁶ LDL receptor-dependent processing is also increased by policosanol treatment.²⁴

The cholesterol-lowering efficacy of policosanol has been proven on patients with type II hypercholesterolemia and on patients with Type 2 diabetes mellitus.²⁷⁻⁴² Results show that policosanol reduces LDL-C, total cholesterol (TC) and the ratios of TC/high-density lipoprotein-cholesterol (HDL-C) and LDL-C/HDL-C, whereas increases HDL-C values.²⁷⁻⁴² Although frequently policosanol reduces triglycerides (TG), its effects have been generally modest and not always consistent.

Postmarketing surveillance studies conducted in more than 30 000 individuals,^{43,44} have also

shown that policosanol is long-term safe and well tolerated.

Two previous studies compared the effects of both policosanol and atorvastatin administered at 10 mg/d for 8 weeks to older hypercholesterolemic and diabetic patients, respectively.^{45,46} Atorvastatin has been more effective than policosanol for lowering LDL-C and TC, TG being similarly reduced by both drugs. Policosanol, but not atorvastatin, has increased HDL-C levels. Both policosanol and atorvastatin were well tolerated, policosanol being better tolerated than atorvastatin.^{45,46}

Taking into account this background, the present study was undertaken to compare the efficacy and tolerability of policosanol and atorvastatin on a broad population of patients with type II hypercholesterolemia.

PATIENTS AND METHODS

Design

This randomized, single-blinded, parallel-group, comparative study was conducted at the Medical Surgical Research Center, the patients being recruited at "Ramón González Coro" Polyclinics (Havana City, Cuba). The study protocol received ethical approval by the independent ethics committee from such centre, written informed consent being obtained from all participants before enrolment.

At recruitment (visit 1) patients entered in a 5 weeks run-in period and were instructed to follow a NCEP step 1 cholesterol-lowering diet.^{16,18} Then, patients attended for lab analyses, being assessed lipid profile variables and blood safety indicators. One-week later patients assisted to visit 2 and those who met study inclusion criteria were randomized, under single-blind conditions, to policosanol (10 mg) or atorvastatin (10 mg) tablets. Study medications were randomized by a fixed randomization method using a block size of 10 and allocation ratio 1:1.

The authors used atorvastatin 10 mg tablets (Cardyl[®]) (Pfizer, SA, Madrid). Policosanol 10 mg-tablets were manufactured to obtain an appearance identical to that of atorvastatin tablets (Laboratorios Dalmer S.A., Havana City, Cuba).

Patients were instructed to take study medications once a day with the evening meal for 8 weeks. After 4 weeks on therapy, an interim checkup was performed (visit 3) and the final checkup was performed at week 8 (visit 4).

Patients

The study enrolled women patients of both sexes, aged 35 to 75 years, with documented hypercholesterolemia. All patients provided written informed consent before enrolling in the trial. Inclusion criteria established the following values after the diet-only period: serum LDL-C levels ≥ 3.4 mmol/L and triglycerides < 4.52 mmol/L. To be included, patients needed to stop any cholesterol-lowering drug for at least 4 weeks before to start the baseline diet only period.

Patients with active renal or hepatic diseases, diagnosed neoplastic diseases and severe hypertension (diastolic pressure ≥ 120 mm Hg) were excluded from the study. In addition, patients who had had a history of unstable angina, myocardial infarction, stroke, transient ischemic attacks or any major surgery within the 3 months prior to the study were also excluded.

Assessments

At enrollment, a complete medical history and physical examination were performed. Physical examination was done from visits 1 to 4. At visits 3 and 4, patients were requested about AE and assessed for compliance with study medications. Compliance was assessed by tablet counts and patient interview. Laboratory tests were reported at baseline and 4 and 8 weeks.

Concomitant medications

The use of any other lipid-lowering drug different than those investigated was prohibited during the study, but no other special prohibition about concomitant medications was established.

Laboratory analysis

Blood samples were drawn from after a 12 h fast and aliquots were taken for laboratory determinations.

Lipid profile. Serum TC and triglycerides were determined by colorimetric enzymatic methods using reagent kits from Roche (Switzerland). Levels of serum HDL-C were determined according to the cholesterol content present in the supernatant obtained after β -lipoproteins precipitation.⁴⁷ LDL-C values were calculated using the Friedewald formula (in mmol/L).⁴⁸

Safety indicators. Other laboratory tolerability tests included determinations of glucose, creatinine, CPK, AST and ALT and were performed by routine laboratory tests

based in enzymatic methods using reagent kits from Roche (Switzerland). All laboratory tests were performed in the Hitachi 719 auto-analyzer (Tokyo, Japan) located at the laboratory of the Center for Surgical and Medical Research (Havana City, Cuba).

Systematic quality control was performed throughout the study, so that the precision and accuracy of the methods were followed.

Efficacy variables

Changes on serum LDL-C levels were considered as primary efficacy variable. The treatments were considered effective only if LDL-C levels were reduced by at least 15 % compared with baseline.⁴⁹ Analyses of the frequency of cases reaching LDL-C goals were also performed. Other lipid profile variables were considered as secondary efficacy variables.

Tolerability

Data from the physical examination, laboratory tests and interview for AE were included for the analysis of drug tolerability. AE predefined as "serious" were fatal or disabling experiences, leading to or prolonging hospitalization, "moderate" were those requiring discontinuation of therapy according to the physician and/or specific treatment of the AE. "Mild" AE were those not requiring withdrawal of study drugs and/or specific treatment of the AE. AE were also classified as unlikely, doubtfully, possibly or probably drug-related according to their estimated relationship with study medications.

Statistical analysis

All data were analyzed by Intention-to-Treat, meaning that data of randomised patients were analysed as randomised, so that data of withdrawals were also included.

For the primary efficacy variable the authors assumed that atorvastatin at 10 mg/d would show a difference in serum LDL-C reduction of 20 % compared with policosanol administered at the same dosage. For that, and based in 95 % test power and 5 % of significance level, a sample size of 160 patients would be enough. Allowing for an estimated dropout rate of 10 %, recruitment of at least 170 patients was needed.

Within group comparisons of continuous variables were performed using the t test for depen-

dent samples; while comparisons between groups were done using the t test for independent samples. Comparison of categorical variables were done using the Fisher's Exact Test. All tests were two tailed. A value of $\alpha = 0.05$ was assumed for statistical significance. Statistical analyses were performed using the Statistica for Windows package program.

RESULTS

Baseline characteristics

One hundred eighty five (185) patients were enrolled for the study, but only 175 were included. Ten patients were not included because their LDL-C values were below inclusion criteria after the diet-only baseline period (7) and TG values remained above 4.52 mmol/L (three patients).

The two groups were well matched with respect all baseline characteristics (Table 1). Study patients showed a very high frequency (≥ 50 %) of arterial hypertension, and a high frequency (≥ 20 %) of diabetes mellitus, smoking. Consumption of concomitant medications was high (> 85 %) and consistent with patient characteristics, since antihypertensive drugs (diuretics, β -adreno-receptor blockers, angiotensin converting enzyme inhibitors (ACEI), calcium channel blockers) and oral hypoglycaemic drugs were among the drugs most frequently consumed by study patients.

Effects on lipid profile

Table 2 summarizes the effects on lipid profile, both groups being well-matched respect all lipid profile variables at randomisation. After 8 weeks, policosanol 10 mg/d significantly ($p < 0.000 001$ vs baseline) lowered LDL-C (27.0 %), TC (19.6 %), LDL-C/high-density lipoprotein-cholesterol (HDL-C) (30.1 %) and TC/HDL-C (23.9 %) ratios, as well as ($p < 0.000 01$) TG (12.4 %). In turn, atorvastatin 10 mg/d decreased ($p < 0.000 001$ vs baseline) LDL-C (35.2 %), TC (26.2 %), LDL-C/HDL-C (34.5 %), TC/HDL-C (25.9 %) and ($p < 0.000 1$) TG (10.2 %). Atorvastatin was more effective than policosanol ($p < 0.001$) to reduce LDL-C and TC ($p < 0.000 1$). Policosanol, but not atorvastatin, significantly increased HDL-C by 10.4 % ($p < 0.000 1$).

At the interim check-up performed at week 4, the changes induced by both drugs on lipid profile were yet significant, the effects of atorvastatin being similar to

Table 1. Baseline characteristics of study patients.

Characteristics	Policosanol (n = 88)		Atorvastatin (n = 87)	
Age (years) (X ± SD)	64 ± 7		63 ± 7	
Body mass index (kg/m ²) (X ± SD)	26.62 ± 3.4		26.44 ± 4.2	
Sex: Female/Males	73/15		73/14	
Personal history				
Hypertension	55	62.5	51	58.6
Diabetes mellitus	26	29.6	28	32.2
Smoking	18	20.4	18	20.7
Obesity (kg/m ² ≥ 30)	14	15.9	15	17.2
CHD	13	14.8	12	13.8
HDL-C < 0,9 mmol/L	4	4.5	2	2.3
Family history of CHD	34	38.6	34	39.1
Concomitant medications* (CM)				
Patients consuming ≥ 1 CM	77	87.5	74	85.1
Diuretics	34	38.6	28	32.2
β-Blockers	16	18.2	17	19.5
Angiotensin converting enzyme inhibitors	16	18.2	13	14.9
Oral hypoglycemic drugs	14	15.9	14	16.1
Calcium channel blockers	9	10.2	11	12.6
Muscular relaxant	9	10.2	10	11.5
Vitamin	9	10.2	10	11.5
Aspirine	10	11.4	5	5.7
Nitrates vasodilators	6	6.8	4	4.6

n Number of patients. CHD Coronary heart disease. (X ± SD) (mean ± standard deviation). The table includes only those CM consumed by ≥ 10 study patients. All comparisons were not significant (Fisher's Exact Probability Test).

those achieved at week 8, while policosanol increased the effects with treatment duration.

Safety and tolerability

Both policosanol and atorvastatin were well tolerated (Table 3). Policosanol, but not atorvastatin, mildly, but significantly lowered systolic blood pressure, but no patient showed symptoms of hypotension and all individual values remained within normal limits. Atorvastatin significantly increased, while policosanol lowered, ALAT and CPK levels respect to baseline.

Six patients withdrew from the study, all from atorvastatin group. Of them, experienced some AE (skin rash, nausea and vomiting, other dyspnea, perspiration and tachycardia, meanwhile the other reported skin rash, myalgia, abdominal pain, uncontrolled hypertension, gastritis, abdominal cramps).

Seventeen patients reported some AE during the study: three policosanol and 14 atorvastatin patients (p < 0.01) who reported a to-

tal of 4 and 23 AE, respectively (Table 4).

DISCUSSION

This study demonstrates that policosanol and atorvastatin, administered at 10 mg/d were effective to lower LDL-C, the main efficacy variable, on patients with type II hypercholesterolemia.

Atorvastatin was more effective than policosanol for lowering LDL-C and TC, a logical result considering that it is more effective than lovastatin, simvastatin, fluvastatin and pravastatin across all dosage ranges,¹⁴⁻²² and that policosanol 10 mg/d was as effective as starting doses of these statins.²⁷⁻⁴² The changes on LDL-C and TC here described are consistent with those independently reported for both atorvastatin²¹ and policosanol.³³⁻³⁵

As occurred in the two previous reports, only policosanol significantly increased HDL-C.^{45,46} In such regard, the effects of atorvastatin 10 mg/d on HDL-C are controversial, so have ranged from modest increases¹⁴⁻¹⁷ to unchanged values.¹⁵⁻²⁰

Thus, the effects here reported for atorvastatin on HDL-C values are over those expected for such dose and treatment duration.

As expected, atorvastatin effectively lowered TG, the decrease obtained being near to that reported for the dose of 10 mg/d.¹⁴⁻²⁰ In turn, the effects of policosanol on TG have been variable, so that they have been significantly reduced in some studies, but unchanged in others.²⁷⁻⁴² As previously reported, atorvastatin and policosanol were similarly effective for decreasing TG.^{45,39}

Both drugs were well tolerated. Atorvastatin significantly, but moderately increased AST and CPK, both changes being expected according to atorvastatin safety and tolerability profile.¹⁴⁻²² Policosanol, by the contrary, significantly reduced both variables, a result consistent with data obtained in previous studies. The significant, but slight reduction of systolic arterial pressure induced by policosanol, not by atorvastatin, also agrees with previous results. This effect, however, is not considered as a potential AE

Table 2. Effects of policosanol (10 mg/d) and atorvastatin (10 mg/d) on lipid profile.

Treatment	Baseline	Week 4	Changes (%)	Week 8	Changes (%)
LDL-C (mmol/L)					
Policosanol	4.42 ± 0.68	3.52 ± 0.69*****	-18.9 ⁺⁺⁺	3.18 ± 0.58*****	-27.0 ⁺
Atorvastatin	4.41 ± 0.66	2.91 ± 0.63****	-33.1	2.82 ± 0.55****	-35.2
TC (mmol/L)					
Policosanol	6.33 ± 0.67	5.40 ± 0.63*****	-14.1 ⁺⁺⁺	5.05 ± 0.56*****	-19.6 ⁺⁺
Atorvastatin	6.32 ± 0.68	4.74 ± 0.69****	-24.3	4.63 ± 0.61****	-26.2
HDL-C (mmol/L)					
Policosanol	1.15 ± 0.25	1.20 ± 0.22	+5.9	1.24 ± 0.23**	+10.4
Atorvastatin	1.15 ± 0.22	1.17 ± 0.30	+1.4	1.17 ± 0.26	+4.1
Triglycerides (mmol/L)					
Policosanol	2.06 ± 0.58	1.79 ± 0.49*	-8.4	1.71 ± 0.48***	-12.4
Atorvastatin	2.05 ± 0.61	1.89 ± 0.58*	-1.4	1.72 ± 0.48**	-10.2
LDL-C/HDL-C					
Policosanol	4.02 ± 1.08	3.06 ± 0.88****	-18.6	2.68 ± 0.72****	-30.1
Atorvastatin	3.99 ± 0.97	2.64 ± 0.83****	-30.7	2.52 ± 0.72****	-34.5
TC/HDL-C					
Policosanol	5.72 ± 1.22	4.63 ± 1.01****	-15.0	4.21 ± 0.85****	-23.9
Atorvastatin	5.68 ± 1.14	4.29 ± 1.02****	-21.9	4.10 ± 0.83****	-25.9

(X ± SD) X Mean. SD Standard deviation. *p < 0.05; **p < 0.001; ***p < 0.000 1; ****p < 0.000 01; *****p < 0.000 001 Comparison with baseline (T-test for dependent samples). ⁺p < 0.01; ⁺⁺p < 0.000 1; ⁺⁺⁺p < 0.000 01; ⁺⁺⁺⁺p < 0.000 001 Comparison with atorvastatin (T-test for independent samples).

since no policosanol-related hypotension has been reported and because the control of arterial pressure is another important goal of coronary prevention. Then, this effect could potentially be an advantage of policosanol, mainly in a population with high frequency of patients with concomitant hypertension and hypercholesterolemia.

The frequency of AE reported in atorvastatin group was higher than that reported by policosanol patients. Thus, the frequency of atorvastatin patients experiencing AE was 14/87 (16.1 %), various patients reporting several AE. Thus, these 14 patients reported 23 AE, indicating that they did not tolerate well the drug. Most of these AE were of gastrointestinal nature, which agrees with the tolerability profile of this drug. Nevertheless, only 3/88 patients randomised to policosanol (3.4 %) referred four AE.

CONCLUSIONS

The present study shows that atorvastatin (10 mg/d) administered for 8 weeks to patients with type II hypercholesterolemia was more ef-

fective than similar doses of policosanol to reduce LDL-C and TC, but similarly effective to reduce TG and both LDL-C/HDL-C and TC/HDL-C ratios. Policosanol, however, but not atorvastatin, was effective to increase HDL-C levels. Policosanol, however, was better tolerated than atorvastatin, as indicated by the changes of ALAT and CPK as well as the AE pattern.

ACKNOWLEDGEMENTS

This study was supported by a research grant from the West Havana Scientific Pole.

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Table 3. Effects of policosanol and atorvastatin on safety indicators.

Treatment	Baseline	Week 4	Week 8
		Body weight (kg)	
Policosanol	68.76 ± 8.43	68.69 ± 8.26	68.63 ± 8.29
Atorvastatin	69.01 ± 11.21	69.42 ± 11.09	69.73 ± 13.70
		Pulse rate (beats/min)	
Policosanol	72.35 ± 6.99	71.67 ± 5.47 ⁺	72.14 ± 5.52 ⁺
Atorvastatin	74.02 ± 6.71	73.52 ± 5.65	74.38 ± 5.89
		SBP (mm Hg)	
Policosanol	129.83 ± 15.69	127.39 ± 14.50 [*]	127.61 ± 14.93 ^{**}
Atorvastatin	129.31 ± 15.68	127.76 ± 19.30	129.26 ± 14.12
		DBP (mm Hg)	
Policosanol	78.92 ± 8.85	77.73 ± 7.84 [*]	78.58 ± 6.99
Atorvastatin	78.02 ± 10.57	9.10 ± 8.45	78.95 ± 7.45
		ALT (U/L)	
Policosanol	19.98 ± 7.31	19.17 ± 6.02 ⁺⁺⁺	18.15 ± 6.20 ⁺⁺⁺⁺
Atorvastatin	20.16 ± 7.80	23.00 ± 7.50 [*]	23.05 ± 9.17 [*]
		AST (U/L)	
Policosanol	24.06 ± 7.47	21.59 ± 6.51 ⁺⁺⁺⁺	20.61 ± 6.81 ⁺⁺⁺⁺
Atorvastatin	24.43 ± 6.99	25.71 ± 7.49	24.51 ± 6.21
		CPK (UI/L)	
Policosanol	99.54 ± 45.80	89.85 ± 36.09 ⁺⁺⁺⁺	86.73 ± 35.29 ⁺⁺⁺⁺
Atorvastatin	102.76 ± 57.75	117.30 ± 58.68 [*]	121.18 ± 54.39 ^{**}
		Glucose (mmol/L)	
Policosanol	5.27 ± 0.95	5.14 ± 0.94	5.14 ± 1.00
Atorvastatin	5.22 ± 0.97	5.19 ± 1.07	5.13 ± 1.04
		Creatinine (µmol/L)	
Policosanol	90.54 ± 14.47	89.17 ± 17.56	88.43 ± 13.84
Atorvastatin	90.64 ± 13.97	89.95 ± 13.57	89.88 ± 16.56

*p < 0.05; ** p < 0.01; *** p < 0.001; **** p < 0.000 1 Comparison with baseline (T-test for dependent samples). ⁺ p < 0.05; ⁺⁺ p < 0.01; ⁺⁺⁺ p < 0.001; ⁺⁺⁺⁺ p < 0.000 1; ⁺⁺⁺⁺⁺ p < 0.000 01 Comparison with atorvastatin (T-test for independent samples).

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Table 4. Effects of policosanol and atorvastatin on safety indicators.

Moderate AE	Policosanol (n = 88)	Atorvastatin (n = 87)
Skin rash	0 (0.0)	2 (2.3)
Uncontrolled hypertension	0 (0.0)	3 (3.4)
Abdominal pain	0 (0.0)	1 (1.2)
Nausea	0 (0.0)	1 (1.2)
Perspiration	0 (0.0)	1 (1.2)
Tachycardia	0 (0.0)	1 (1.2)
Dyspnea	0 (0.0)	1 (1.2)
Myalgia	0 (0.0)	1 (1.2)
Migraine	0 (0.0)	1 (1.2)
Gastritis	0 (0.0)	1 (1.2)
Vomiting	0 (0.0)	1 (1.2)
Insomnia	1 (1.2)	0 (0.0)
Pruritus	1 (1.2)	0 (0.0)
Arthralgia	1 (1.2)	0 (0.0)
Total of moderate AE	3 (3.5)	14 (16.1) ⁺⁺
Mild AE		
Headache	1 (1.2)	0 (0.0)
Asthenia	0 (0.0)	2 (2.3)
Skin rash	0 (0.0)	1 (1.2)
Abdominal pain	0 (0.0)	1 (1.2)
Cramps	0 (0.0)	1 (1.2)
Insomnia	0 (0.0)	1 (1.2)
Abdominal cramps	0 (0.0)	1 (1.2)
Lower limb pain	0 (0.0)	1 (1.2)
Uncontrolled hypertension	0 (0.0)	1 (1.2)
Total of mild AE	1 (1.2)	9 (10.3) ⁺⁺
Total of AE	4 (4.5)	23 (26.4) ⁺⁺⁺
Total of patients reported EA	3 (3.4)	14 (16.1) ⁺⁺

⁺⁺ p < 0.01; ⁺⁺⁺ p < 0.001 Comparison with policosanol (χ^2 test).

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RESULTADOS CIENTIFICOS DESTACADOS MINISTERIO DE EDUCACION SUPERIOR DE CUBA

EMPLEO GENERALIZADO DE LA CORALINA® HAP-200 EN TODO EL PAIS EN ESTOMATOLOGIA Y CIRUGIA MAXILOFACIAL

Laboratorio de Biomateriales, Centro Nacional de Investigaciones Científicas.

La hidroxiapatita porosa Coralina® HAP-200 es un biomaterial para implantes óseos desarrollado a finales de la década del ochenta, el cual constituye el primer biomaterial grado III según la clasificación internacional que se desarrolla y aplica en Cuba.

En 1992, este producto obtuvo certificado de registro sanitario en el país para aplicaciones en Estomatología y Cirugía Maxilofacial. Actualmente, se cuenta con las instalaciones adecuadas y la capacidad productiva necesaria para satisfacer toda la demanda nacional y los planes de exportación en condiciones de Buenas Prácticas de Producción.

Se produce a partir de corales marinos, los cuales han resultado excelentes fuentes para la obtención de materiales biocompatibles con los huesos, ya que los procesos biológicos que tienen lugar en ellos constituyen modelos de perfecta organización anatómica y fisiológica. Todo el proceso de prospección y colecta de corales se realiza a través de los organismos especializados y autorizados para el control del medio ambiente, con lo cual, se garantiza su explotación de forma sostenible sin dañar el ecosistema.

No se conocen contraindicaciones en el uso de Coralina® HAP-200.

A partir de 1990, se comenzó a suministrar estos biomateriales a hospitales de varias provincias del país con vistas a realizar diferentes protocolos de ensayos y estudios clínicos y a partir de 2000, se inició su comercialización.

Los volúmenes del producto puesto a disposición de las instituciones de Salud del país han permitido tratar un número creciente de pacientes cada año. En los dos últimos, se apreció un incremento considerable en su aplicación. Hasta el presente, se han tratado unos 9 600 pacientes, de ellos, 4 300 en los dos últimos años.

Las lesiones tratadas en esta especialidad abarcan desde pequeños defectos de los huesos en el maxilar y la mandíbula, hasta grandes pérdidas óseas en la regiones facial y craneal con grandes deformaciones y secuelas estéticas y funcionales.

Cuba es uno de los pocos países en el mundo que pone este tipo de producto a plena disposición de toda la población, lo que eleva la calidad de los servicios médicos especializados en implantología y cirugía reconstructiva y contribuye a mejorar la calidad de vida de aquella.

En el desarrollo y generalización de este producto, se ha contado con la colaboración de especialistas, estomatólogos, cirujanos maxilofaciales y autoridades de importantes instituciones de Salud Pública del país.



GRANULADOS



RECTANGULARES



CIRCULARES



ESFERICAS