Comparison of the effects of policosanol and atorvastatin on postmenopausal women with type II hypercholesterolemia

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Palabras clave: hipercolesterolemia, postmenopáusicas, policosanol, atorvastatina.

Key words: hypercholesterolemia, postmenopausal woman, policosanol, atorvastatin.

RESUMEN. Las mujeres postmenopáusicas presentan concentraciones mayores de colesterol total (CT) y del transportado por lipoproteínas de baja densidad (LDL-C) y menores del transportado por lipoproteínas de alta densidad (HDL-C) que las premenopáusicas. Analizar su dislipidemia implica reducir las concentraciones de las LDL-C. El policosanol (5 a 20 mg/d) es un hipocolesterolemizante efectivo y la atorvastatina (10 a 80 mg/d) una de las estatinas más efectivas. Este estudio, aleatorizado y a simple-ciegas, comparó la eficacia y tolerabilidad del policosanol y la atorvastatina en mujeres postmenopáusicas con hipercolesterolemia. Tras un periodo basal de dieta, 60 mujeres recibieron policosanol o atorvastatina 10-mg/d, durante 8 semanas. El policosanol y la atorvastatina redujeron significativamente (p < 0.001) las concentraciones de LDL-C (32,8 y 39,7 %, respectivamente), CT (23,6 y 29,1 %) y (p < 0,001) TG (11,3 y 17,6 %), y aumentaron (p < 0,001) las de HDL-C (11,3 % y 9,9 %, respectivamente). La atorvastatina fue más efectiva en reducir (p < 0,001) LDL-C, CT y (p < 0,05) TG. Ambos tratamientos fueron bien tolerados. La atorvastatina aumentó significativamente (p < 0,01) y el policosanol redujo (p < 0,05) las transaminasas y la creatinofosfoquinasa. Tres pacientes tratados con atorvastatina, causaron baja por experiencias adversas. Con atorvastatina (cinco pacientes) estas fueron más frecuentes que con policosanol (un paciente). El tratado con policosanol refirió dolor de cabeza, los de atorvastatina refirieron erupción (3), taquicardia (1), náuseas (1), vómitos (1), dolor abdominal (1), calambres (1), disnea (1) y sudoración (1). En conclusión, ambos tratamientos, administrados a 10 mg/d por 8 semanas a mujeres postmenopáusicas hipercolesterolemáticas, modificaron favorablemente el perfil lipídico, la atorvastatina fue más efectiva en reducir LDL-C, CT y TG, y el policosanol mejor tolerado.

ABSTRACT. Postmenopausal women show elevated serum low-density lipoprotein-cholesterol (LDL-C), total cholesterol (TC), and low high-density lipoprotein-cholesterol (HDL-C) compared with premenopausal women, and to control their dyslipidemia means to lower LDL-C levels. Policosanol (5 to 20 mg/d) is an effective cholesterol-lowering agent, and atorvastatin (10 - 80 mg/d) one of the most efficacious statins. This randomized, single-blinded study compared the efficacy and tolerability of policosanol and atorvastatin in postmenopausal women with type II hypercholesterolemia. After a baseline cholesterol-lowering diet step, 60 patients were randomized to policosanol or atorvastatin 10-mg/d for 8 weeks. Policosanol and atorvastatin significantly (p < 0.001) lowered LDL-C (32.8 and 39.7 %, respectively), TC (23.6 and 29.1 %) and (p < 0.001) TG (11.3 and 17.6 %), whereas significantly increased (p < 0.001) HDL-C (11.3 % and 9.9 %, respectively). Atorvastatin was more effective (p < 0.001) than policosanol to reduce LDL-C, CT and (p < 0.05) TG. Both drugs were well tolerated. Aторвастатин significantly increased (p < 0.01), while policosanol lowered (p < 0.05) transaminase and creatinokinase levels. Three patients, all from atorvastatin, withdrew from the trial due to adverse experiences (AE). The AE with atorvastatin (five patients) were more frequent than with policosanol (one patient). The policosanol-patient reported headache, the atorvastatin patients referred rash (3), tachycardia (1), nausea (1), vomiting (1), abdominal pain (1), muscle cramps (1), dyspnea (1) and perspiration (1). In conclusion, both treatments, at 10 mg/d for 8 weeks, favourably changed the lipid profile in postmenopausal hypercholesterolemic women, atorvastatin being more effective for lowering LDL-C, CT, TG, and policosanol better tolerated.

INTRODUCTION

Coronary heart disease (CHD) is the major cause of mortality in adults.1 Hypercholesterolemia associated with elevated plasma low-density lipoprotein cholesterol (LDL-C) is a major CHD risk factor,2,3 and endpoint clinical studies have proven the clinical benefits of lowering elevated plasma LDL-C levels.2,13

Premenopausal women have a frequency of coronary events lower than men of similar age, but such difference is further attenuated, CHD increases in women with aging.14,15 Postmenopausal women commonly show elevated plasma levels of LDL-C and total cholesterol (TC), moderately increased triglycerides (TG), whereas high-density lipoprotein-cholesterol (HDL-C) decreased moderately.14,16 Clinical studies have demonstrated that lowering LDL-C significantly decreases coronary events in patients with and without previous CHD history, these benefits being observed in both men and women.7-13

Expert guidelines recommend treat hypercholesterolemia in postmenopausal women as a part of the coronary prevention strategy.2,3 Concurrence of multiple risk factors increases the global coronary risk and LDL-C goals, the cornerstone of hypercholesterolemia management, become more restrictive for individuals at highest
risk, like 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 dyslipidaemia management, which applies for postmenopausal women,2,3 but such measures alone are often not enough to reach a desirable control. Then, cholesterol-lowering drugs should be indicated to these patients, HMGCoA reductase inhibitors being a first-choice alternative for lowering serum LDL-C in postmenopausal women.2,3

Atorvastatin is a statin that, across its dosage range (10 - 80 mg/d), induces reductions of serum LDL-C greater than with simvastatin, pravastatin, lovastatin, fluvastatin and cerivastatin.17-24 Atorvastatin has been shown as effective and safe for treating hypercholesterolemia in postmenopausal women.24 Thus, it is a suitable reference to compare the cholesterol-lowering effects of any other hypcholesterolemic drug. Atorvastatin is generally well tolerated and most drug-related adverse events (AE) are mild and transient, gastrointestinal AE being the most frequent. As for other statins, persistent increases on serum transaminases and creatinphosphokinase (CPK), myalgia and myopathy have been reported for atorvastatin.17,20

Policosanol is a mixture of higher aliphatic primary alcohols purified from sugar cane wax26 with cholesterol-lowering effects that inhibits cholesterol biosynthesis before mevalonate production,27-29 through regulating HMG CoA reductase activity,29,30 and also increases the LDL receptor-dependent processing.27 Policosanol has been shown to lower LDL-C in patients with type II hypercholesterolemia and in patients with type 2 diabetes mellitus,31-46 being also effective, as safe and well tolerated in hypercholesterolemic postmenopausal women.37-39 Postmarketing surveillance studies in more than 30,000 individuals,47,48 corroborate that policosanol is long-term safe and well tolerated.

Two previous studies compared the effects of policosanol and atorvastatin at 10 mg/d for 8 weeks in older hypercholesterolemic and diabetic patients, respectively.22,43 Atorvastatin was more effective than policosanol for lowering LDL-C and TC, but both drugs lowered similarly serum triglycerides (TG), while policosanol, not atorvastatin, has raised HDL-C levels. Both drugs were well tolerated, but policosanol better than atorvastatin.22,43

In light of this background, this study compared the efficacy and tolerability of policosanol and atorvastatin on postmenopausal women with type II hypercholesterolemia.

PATIENTS AND METHODS

Design

This randomized, single-blinded, parallel-group, comparative study was conducted at the Medical Surgical Research Centre. The study protocol received ethical approval by the independent ethics committee from such centre, written informed consent being obtained from all participants before their enrolment at “Ramón González Coro” Policlinics Havana City, Cuba.

At recruitment (visit 1) patients entered in a five weeks run-in period, being instructed to follow a NCEP step 1 cholesterol-lowering diet.36,38 Then, lipid profile was determined, and aliquots for other laboratory determinations taken. One-week later eligible patients were randomized, under single-blind conditions, to policosanol (10 mg) or atorvastatin (10 mg) tablets (visit 2).

Study drugs were randomized through a fixed randomization method, using a block size of 10 and allocation ratio 1 : 1. It was used atorvastatin 10 mg tablets (Cardyl®)(Pfizer, S.A., 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 fourweeks on therapy, an interim check-up was performed (visit 3) and the final check-up was performed at week eight (visit 4).

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.

Patients

The study enrolled women at least one year of persistent amenorrhea and documented type II 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 (TG) ≤ 4.52 mmol/L.

Patients with active renal or hepatic diseases, diagnosed neoplasic 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 three months prior to the study were also excluded.

Concomitant medications

The use of any other lipid-lowering drug different from those researched 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.

Serum TC and TG levels were determined with enzymatic methods and reagent kits (Roche, Switzerland), and serum HDL-C as the cholesterol content in the supernatant obtained after precipitating β-lipoproteins.14 LDL-C values were calculated using the Friedewald formula.40

Other laboratory tolerability indicators (glucose, creatinine, CPK, AST and ALT) were assessed through routine enzymatic methods and reagent kits from the same company. All laboratory tests were performed in the Hitachi 719 autoanalyzer (Tokyo, Japan) located at 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. Precision was assessed according to repeatability (r) (within-day variations) and reproducibility (R) (between-day variations); and accuracy against standard references.

Efficacy variables

Reduction of serum LDL-C levels was the primary efficacy variable. The treatments were considered effective only if LDL-C levels were reduced by at least 15 % compared with baseline.14 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 hospitalization and/or deaths, “moderate” those requiring discontinuation of therapy and/or specific treatment of the AE, and mild AE those not requiring withdrawal of study drugs and/or specific treatment of the AE.

Statistical analysis

All data were analyzed as per Intention-to-Treat, meaning that data of randomised patients were analysed as randomised. For the primary efficacy variable it was 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 80 % test power and 5 % of significance level, a sample size of 60 patients would be enough. Allowing for an estimated dropout rate of 10 %, recruitment of at least 66 patients was needed.

Continuous variables were compared within the groups with the Wilcoxon test for paired samples; and between groups with the Mann Whitney U test. Categorical variables were compared with the Fisher’s exact test. All tests were two tailed. A value of α = 0.05 was assumed for statistical significance. Statistical analyses were performed with the software Statistics for Windows.

RESULTS

Baseline characteristics

Sixty-seven patients were enrolled, but only 60 were eligible. Seven patients were not included because of LDL-C values were below inclusion criteria after the diet-only baseline period. The two groups were well matched with regards to all baseline characteristics (Table 1). Study patients showed a high frequency of arterial hypertension and family history of CHD. Consumption of concomitant medications was relatively high and consistent with patient characteristics since antihypertensive drugs were among the drugs most frequently consumed by study patients.

Effects on lipid profile

After eight weeks, policosanol and atorvastatin significantly (p < 0.000 01) lowered LDL-C (32.8 and 39.7 %, respectively), TC (23.6 and 29.1 %) and (p < 0.001) TG (11.3 and 17.6 %), whereas they significantly increased (p < 0.000 1 and p < 0.001) HDL-C (11.3 and 9.9 %, respectively). Atorvastatin was more effective (p < 0.001) than policosanol to reduce LDL-C, TC and (p < 0.05) TG. At week 4, the changes induced by both drugs on lipid profile were yet significant, the effects of atorvastatin on LDL-C and TC being similar to those achieved at week 8, while policosanol increased these effects with treatment duration (Table 2).

Safety and tolerability

Both policosanol and atorvastatin were well tolerated. Policosanol, but not atorvastatin, mildly, but significantly lowered both systolic and diastolic blood pressure, but no patient showed symptoms of hypotension and all individual values remained within normal limits. Atorvastatin significantly increased (p < 0.01), while policosanol lowered (p < 0.05) ALT and CPK levels respect to baseline (Table 3).

Three patients withdrew from the study due to AE, all from atorvastatin group. One experienced skin rash, nausea and vomiting, other dyspnea, perspiration and tachycardia, meanwhile the other reported skin rash.

Table 1. Baseline characteristics of study patients.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Policosanol (n = 30)</th>
<th>Atorvastatin (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)(X ± SD)</td>
<td>63 ± 6</td>
<td>63 ± 8</td>
</tr>
<tr>
<td>Body mass index (kg/m²)(X ± SD)</td>
<td>25.2 ± 2.9</td>
<td>25.2 ± 3.3</td>
</tr>
<tr>
<td>Personal history n %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>22 73.3</td>
<td>20 66.0</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>4 13.3</td>
<td>5 16.7</td>
</tr>
<tr>
<td>CHD</td>
<td>3 10.0</td>
<td>4 13.3</td>
</tr>
<tr>
<td>Smoking</td>
<td>3 10.0</td>
<td>4 13.3</td>
</tr>
<tr>
<td>Obesity (kg/m² ≥ 30)</td>
<td>1 3.3</td>
<td>3 10.0</td>
</tr>
<tr>
<td>Family history of CHD</td>
<td>14 46.7</td>
<td>12 40.0</td>
</tr>
<tr>
<td>Concomitant medications (CM)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diuretics</td>
<td>16 53.3</td>
<td>12 40.0</td>
</tr>
<tr>
<td>β-blockers</td>
<td>7 23.3</td>
<td>7 23.3</td>
</tr>
<tr>
<td>Angiotensin converting enzyme inhibitors</td>
<td>7 23.3</td>
<td>5 16.7</td>
</tr>
<tr>
<td>Meprobamate</td>
<td>3 10.0</td>
<td>5 16.7</td>
</tr>
<tr>
<td>Oral hypoglycemic drugs</td>
<td>3 10.0</td>
<td>3 10.0</td>
</tr>
<tr>
<td>Nitrates vasodilators</td>
<td>2 6.7</td>
<td>4 13.3</td>
</tr>
<tr>
<td>Calcium antagonists</td>
<td>2 6.7</td>
<td>3 10.0</td>
</tr>
</tbody>
</table>

n Number of patients. CHD coronary heart disease. (X ± SD) (mean ± standard deviation). 1 The table includes only those CM consumed by ≥ five study patients. All comparisons were not significant (Fisher’s exact probability test).
Table 2. Effects of policosanol and atorvastatin (10 mg/d) on lipid profile.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Baseline</th>
<th>Week 4</th>
<th>Changes (%)</th>
<th>Week 8</th>
<th>Changes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(X ± SD)</td>
<td></td>
<td></td>
<td>(X ± SD)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(mean ± standard deviation)</td>
<td></td>
<td></td>
<td>(mean ± standard deviation)</td>
<td></td>
</tr>
<tr>
<td>LDL-C (mmol/L)</td>
<td>Policosanol</td>
<td>4.79 ± 0.48</td>
<td>3.66 ± 0.50</td>
<td>**</td>
<td>−22.1***</td>
</tr>
<tr>
<td></td>
<td>Atorvastatin</td>
<td>4.63 ± 0.60</td>
<td>2.79 ± 0.53</td>
<td>**</td>
<td>−39.3</td>
</tr>
<tr>
<td>TC (mmol/L)</td>
<td>Policosanol</td>
<td>6.60 ± 0.52</td>
<td>5.54 ± 0.52</td>
<td>**</td>
<td>−15.9***</td>
</tr>
<tr>
<td></td>
<td>Atorvastatin</td>
<td>6.44 ± 0.63</td>
<td>4.59 ± 0.54</td>
<td>**</td>
<td>−28.3</td>
</tr>
<tr>
<td>HDL-C (mmol/L)</td>
<td>Policosanol</td>
<td>1.04 ± 0.08</td>
<td>1.09 ± 0.06</td>
<td>*</td>
<td>+5.5</td>
</tr>
<tr>
<td></td>
<td>Atorvastatin</td>
<td>1.05 ± 0.04</td>
<td>1.10 ± 0.09</td>
<td>*</td>
<td>+5.5</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>Policosanol</td>
<td>2.08 ± 0.37</td>
<td>1.85 ± 0.30</td>
<td>**</td>
<td>−9.7</td>
</tr>
<tr>
<td></td>
<td>Atorvastatin</td>
<td>2.07 ± 0.35</td>
<td>1.82 ± 0.26</td>
<td>**</td>
<td>−12.2</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Baseline</th>
<th>Week 4</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(X ± SD)</td>
<td></td>
<td>(X ± SD)</td>
</tr>
<tr>
<td></td>
<td>(mean ± standard deviation)</td>
<td></td>
<td>(mean ± standard deviation)</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>Policosanol</td>
<td>66.20 ± 7.59</td>
<td>66.28 ± 7.55</td>
</tr>
<tr>
<td></td>
<td>Atorvastatin</td>
<td>65.93 ± 8.84</td>
<td>66.91 ± 8.90</td>
</tr>
<tr>
<td>Pulse rate (beats/min)</td>
<td>Policosanol</td>
<td>69.17 ± 4.32</td>
<td>69.40 ± 2.53</td>
</tr>
<tr>
<td></td>
<td>Atorvastatin</td>
<td>70.53 ± 5.32</td>
<td>70.37 ± 2.78</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>Policosanol</td>
<td>130.67 ± 9.80</td>
<td>128.67 ± 7.76</td>
</tr>
<tr>
<td></td>
<td>Atorvastatin</td>
<td>130.67 ± 8.28</td>
<td>128.52 ± 7.18</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>Policosanol</td>
<td>81.33 ± 5.71</td>
<td>79.00 ± 3.05*</td>
</tr>
<tr>
<td></td>
<td>Atorvastatin</td>
<td>80.67 ± 6.40</td>
<td>79.63 ± 5.17</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>Policosanol</td>
<td>20.73 ± 6.91</td>
<td>19.53 ± 5.41*</td>
</tr>
<tr>
<td></td>
<td>Atorvastatin</td>
<td>18.23 ± 5.19</td>
<td>22.93 ± 5.08***</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>Policosanol</td>
<td>24.67 ± 6.35</td>
<td>22.13 ± 3.77*</td>
</tr>
<tr>
<td></td>
<td>Atorvastatin</td>
<td>23.47 ± 4.80</td>
<td>25.41 ± 5.71*</td>
</tr>
<tr>
<td>CPK (U/L)</td>
<td>Policosanol</td>
<td>93.43 ± 39.40</td>
<td>83.77 ± 28.77***</td>
</tr>
<tr>
<td></td>
<td>Atorvastatin</td>
<td>93.43 ± 38.73</td>
<td>117.93 ± 38.25**</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>Policosanol</td>
<td>5.25 ± 0.68</td>
<td>5.32 ± 0.57</td>
</tr>
<tr>
<td></td>
<td>Atorvastatin</td>
<td>5.37 ± 0.83</td>
<td>5.34 ± 0.60</td>
</tr>
<tr>
<td>Creatinine (µmol/L)</td>
<td>Policosanol</td>
<td>90.07 ± 12.40</td>
<td>86.83 ± 8.94</td>
</tr>
<tr>
<td></td>
<td>Atorvastatin</td>
<td>89.17 ± 13.38</td>
<td>88.48 ± 10.69</td>
</tr>
</tbody>
</table>
and pravastatin across all dosage range, more effective than lovastatin, simvastatin, fluvastatin. LDL-C and TC, a logical result considering that it is LDL-C, the main efficacy variable, in postmenopausal atorvastatin, at 10 mg/d for 8 weeks, were effective to lower DISCUSSION (Tabla 4).

of these AE, all in atorvastatin group, were moderate

Differently from the two previous comparative studies versus atorvastatin, in which only policosanol increased significantly HDL-C, here both drugs induced similar HDL-C increases. In such regard, the effects of atorvastatin 10 mg/d on HDL-C are controversial, so they have ranged from modest increases to unchanged values. Thus, the effects here reported for atorvastatin on HDL-C values are over those expected for such dose and treatment duration, a finding without conclusive explanation.

As expected, atorvastatin effectively lowered TG, the decrease obtained being near to that reported for the dose of 10 mg/d. In turn, the effects of policosanol on TG have been variable, so that TG are significantly reduced in some studies, but unchanged in others.

Atorvastatin was more effective than policosanol for reducing TG, as expected, although in the two previous comparative studies conducted with policosanol 10 mg/d versus atorvastatin 10 mg/d both drugs have induced similar effects on TG.

Both drugs were well tolerated. Atorvastatin increased ALT and CPK moderately, but significantly, consistent with the atorvastatin safety profile. Policosanol, on the contrary, significantly reduced both variables, as in some previous studies.

The significant, but slight reduction of arterial pressure induced with policosanol, not with atorvastatin, also agrees with previous data. This effect, however, is not considered a potential AE, no policosanol-related hypotension has been found, and to control arterial pressure is also important for coronary prevention. Then, this effect could be a potential benefit of policosanol in a population with a high frequency of concomitant hypertension and hypercholesterolemia.

The frequency of AE reported in atorvastatin was greater than in policosanol group. In particular, the frequency of moderate AE in atorvastatin group was relatively high (5/30, 16.7%), various patients referring more than one AE. Thus, these five patients reported 10 AE, indicating that they did not tolerate well the drug. In policosanol group only one patient referred a mild AE. Most of these AE were of gastrointestinal nature, which agrees with the tolerability profile of this drug.

CONCLUSIONS

The present study shows that both policosanol and atorvastatin at 10 mg/d for eight weeks, favourably changed the lipid profile in postmenopausal hypercholesterolemic women, atorvastatin being more effective for lowering LDL-C, TC, TG, and policosanol better tolerated.

**TABLE 4. Adverse events (AE) reported by study patients.**

<table>
<thead>
<tr>
<th></th>
<th>Policosanol (n = 30)</th>
<th>Atorvastatin (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Moderate AE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin rash</td>
<td>0 (0.0)</td>
<td>2 (6.7)</td>
</tr>
<tr>
<td>Nausea</td>
<td>0 (0.0)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>0 (0.0)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Perspiration</td>
<td>0 (0.0)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>0 (0.0)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>0 (0.0)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>0 (0.0)</td>
<td>7 (23.3)**</td>
</tr>
<tr>
<td><strong>Mild AE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>1 (3.3)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Skin rash</td>
<td>0 (0.0)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>0 (0.0)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Muscle cramps</td>
<td>0 (0.0)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Subtotal AE</td>
<td>1 (3.3)</td>
<td>3 (1.0)</td>
</tr>
<tr>
<td>Total of AE</td>
<td>1 (3.3)</td>
<td>10 (33.3)**</td>
</tr>
<tr>
<td><strong>Total of patients reported EA</strong></td>
<td>1 (3.3)</td>
<td>5 (16.7)</td>
</tr>
</tbody>
</table>

++ p < 0.01 Comparison with atorvastatin (Fisher’s exact probability test).

The AE in atorvastatin were more frequent (p < 0.01) than in policosanol group. Six patients (1 policosanol, 5 atorvastatin) reported 10 AE: the policosanol-treated patient experienced headache, while the atorvastatin treated patients reported skin rash (3), tachycardia (1), nausea (1), vomiting (1), abdominal pain (1), muscle cramps (1), dyspnea (1) and perspiration (1). Seven of these AE, all in atorvastatin group, were moderate (Tabla 4).

BIBLIOGRAPHY


