Lipid lowering effect of policosanol and omega-3 fatty acids combined therapy in hypercholesterolemic patients

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RESUMEN. Aunque el colesterol de las lipoproteínas de baja densidad (LDL-C) continúa siendo el principal objetivo en el manejo de la dislipidemia, la prevención de la enfermedad coronaria incluye además, la modificación de otros indicadores tales como la disminución del colesterol no unido a las lipoproteínas de alta densidad y los triglicéridos séricos (TG), así como el incremento de las HDL-C. Se reconoce que los aceites de pescado ricos en ácidos grasos omega 3 (AG-ω3), los cuales reducen los TG séricos y el colesterol no unido a HDL, pueden disminuir el riesgo de los eventos cardiovasculares a través de estos efectos y a través de otros efectos no relacionados con los lípidos (reducción de la frecuencia cardiaca, efectos antiarrítmicos, discreta reducción de la hipertensión arterial y de la agregación plaquetaria). El efecto de AG-ω3 sobre las HDL y el colesterol total (CT) puede ser variable y en ocasiones tiende a incrementar las concentraciones de las LDL-C en el suero. El policosanol ha demostrado que reduce las LDL-C y CT mientras que incrementa las HDL-C en individuos normocolesterolémicos e hiperlipidémicos, con un efecto marginal e inconsistente sobre los triglicéridos. El policosanol administrado concomitantemente con ω-3-FA durante un corto período demostró que reduce la LDL-C y el CT mientras que aumenta las HDL-C más que el placebo AG-ω3 + placebo, sin afectar el efecto reductor de los TG de los AG-ω3. No se ha reportado, sin embargo, la persistencia de tales efectos. Este estudio investiga si los beneficios de la administración de AG-ω3 + policosanol (AG-ω3-poli) persisten después de una terapia más prolongada (24 semanas). Después de un periodo de dieta solamente, 60 pacientes se distribuyeron, aleatoriamente y a doble ciegas, en dos grupos. Uno de los grupos fue tratado con AG-ω3 (1 g/d) + placebo (AG-ω3-pla) mientras que el otro recibió AG-ω3 (1 g/d) + policosanol 10 mg/d . Las variables de laboratorio fueron evaluadas al inicio y cada 12 semanas mientas que los indicadores del examen físico, la tolerabilidad y las experiencias adversas fueron controlados cada seis semanas. Después de 12 semanas de tratamiento con AG-ω3-pla, los TG se redujeron significativamente ($p > 0,000\ 1$) con respecto a los valores iniciales (15,8 %) mientras que a las 24 semanas disminuyeron ($p < 0,000\ 1$), (22,8 %) y se observó un incremento de HDL-C ($p < 0,05$), (1,4 %), sin cambios en otras variables lipídicas. A las semanas 12 y 24, AG-ω3-poli redujo ($p < 0,000\ 1$) LDL-C (23,4 y 26,0 %, respectivamente), TC (15,4 y 16,6 %) y aumento HDL-C (9,0 y 14,5 %) comparado con el valor inicial y con AG-ω3 + placebo, mientras que disminuyó ($p < 0,000\ 1$) los TG (16,7 y 23,3 %, respectivamente) contra los valores iniciales, pero no contra AG-ω3 + placebo. No se produjo ninguna salida del estudio. Siete pacientes reportaron EA ligeras, sin diferencias entre los grupos. En conclusión, la terapia combinada AG-ω3-poli durante 24 semanas demostró beneficios complementarios persistentes sobre el perfil de los lípidos séricos comparado con AG-ω3 + placebo y fue bien tolerado por los pacientes hipercolesterolémicos.

ABSTRACT. Although low-density lipoprotein cholesterol (LDL-C) remains the primary treatment target, the management of dyslipidemia for the coronary prevention includes the modification of secondary lipid targets, like the decrease of non-high-density lipoprotein cholesterol (HDL-C) and serum triglycerides (TG), and the increase of serum HDL-C. It has been acknowledged that fish oils rich in omega-3 fatty acids (ω-3-FA), which reduce serum TG and non-HDL-C levels, may decrease the risk of cardiovascular events through these lipid and through non-lipid (reduction of pulse rate, antiarrythmic effects, modest decreases of blood pressure and of platelet aggregation) mechanisms. While their effects on serum HDL-C and total cholesterol (TC) have been variable, treatment with ω-3-FA, however, may sometimes increase serum LDL-C levels. Policosanol has been shown to reduce serum LDL-C, TC and to increase HDL-C in normocholesterolemic and hyperlipidemic individuals, without marginal and inconsistent effects on TG. Policosanol administered concomitantly with ω-3-FA for short-term has been shown to reduce serum LDL-C, TC and to raise HDL-C more than ω-3-FA + placebo, unaffecting the TG-lowering effect of ω-3-FA. No information of the persistence of such effects, however, has been reported. This study investigated whether the benefits of administering ω-3-FA + policosanol (ω-3-FA-poli) persisted after longer (24 weeks) therapy. After a diet-only period, 60 patients were randomized, under double-blind conditions, to ω-3-FA (1 g/d) + placebo (ω-3-FA-pla) or ω-3-FA (1 g/d) + policosanol 10 mg/d . Laboratory variables were assessed at baseline and every 12 weeks, while physical indicators, drug compliance and adverse experiences (AE) were controlled every six

weeks. After 12 weeks on therapy, treatment with ω-3-FA-pla reduced significantly ($p < 0.000\ 1$) TG (15.8 %) compared with baseline, while at week 24 significant ($p < 0.000\ 1$) decreases of TG (22.8 %) and increases ($p < 0.05$) of HDL-C (1.4 %) were seen, without changes on other lipid variables. At weeks 12 and 24, ω-3-FA-poli reduced ($p < 0.000\ 1$) LDL-C (23.4 and 26.0 %, respectively), TC (15.4 and 16.6 %) and raised HDL-C (9.0 and 14.5 %) compared with baseline and -3-FA + placebo, while lowered ($p < 0.0001$) serum TG (16.7 and 23.3 %, respectively) *versus* baseline, but not *versus* ω-3-FA + placebo. There were not study withdrawals. Seven patients reported mild AE, without differences between both groups. In conclusion, combined therapy with ω-3-FA-poli given for 24 weeks showed complementary and persistent benefits on lipid profile targets compared ω-3-FA + placebo, and was well tolerated in hypercholesterolemic patients.

INTRODUCTION

Elevated serum low-density lipoprotein (LDL-C) and total (TC) cholesterol levels are coronary risk factors[1] whose reduction has been shown to lower coronary events.[2-7] As reported in the National Cholesterol Education Program Adult Treatment Panel III guidelines, LDL-C remains the primary target of dyslipidemia management for reducing the coronary risk,[8] but the modification of secondary lipid targets like the reduction of triglycerides (TG), non-high-density lipoprotein cholesterol (HDL-C) and the increase of high-density lipoprotein cholesterol (HDL-C) are needed in high-risk patients. Therapeutic lifestyle changes, which include the adherence to a standard cholesterol-lowering diet, are encouraged as the first-choice option to treat dyslipidemia. Diet alone, however, frequently is not enough to achieve the LDL-C goals, mainly in high risk patients that require more restrictive targets. In these cases, lipid-lowering drugs should be indicated.[8]

Fish oils, rich in omega-3 long-chain polyunsaturated fatty acids (ω-3-FA), mainly eicosapentanoic (EPA) and docosahexaenoic (DHEA) acids, are currently recommended for cardiovascular prevention. It has been acknowledged that ω-3-FA may decrease the risk of cardiovascular events through non-lipid (antiarrythmic effects, reduction of pulse rate, modest decreases of blood pressure and of platelet aggregation) and lipid mechanisms (reduction of both serum TG and non-HDL-C levels). Treatment with ω-3-FA, however, may sometimes increase serum LDL-C, meanwhile their effects on serum HDL-C and total cholesterol (TC) have been variable.[9-17] Therapy with ω-3-FA has been shown to be safe and well tolerated.[18]

Policosanol is a mixture of eight high molecular weight alcohols with cholesterol-lowering and antiplatelet effects demonstrated in normocholesterolemic and dyslipidemic subjects.[19-41] Likewise, policosanol has shown to be short[19-36] and long-term[37-41] safe and well tolerated.

A meta-analysis of 29 randomized controlled trials compared the effects of policosanol and other natural lipid-lowering therapies found a 23.7 % estimated LDL-C reduction with policosanol (5-40 mg/d, 1 528 patients) and 0.11 % with placebo (1 406 patients) (cumulative $p < 0.000\ 1$), concluding that policosanol was effective, safe and well tolerated.[42]

Combination therapies with ω-3-FA and other lipid-lowering therapies have been shown to beneficially modify the lipid profile.[43,44] Considering the distinct effects of ω-3-FA and policosanol on the lipid profile, which should be complementary, previous studies investigated whether the therapy with ω-3-FA + policosanol (ω-3-FA-poli) provided greater benefits on the lipid profile than ω-3-FA + placebo (ω-3-FA-pla), demonstrating that such combined therapy reduced LDL-C and TC levels, and increased HDL-C values more than ω-3-FA-pla, while unchanged the TG-lowering effect of ω-3-FA,[45,46] but they did not explore, however, the effects of such combined therapy given for more than eight weeks.

In light of these issues, the purpose of this study is to investigated whether ω-3-FA-poli given for 24 weeks produced persistent benefits on the lipid profile of hypercholesterolemic patients compared with ω-3-FA-pla.

PARTICIPANTS AND METHODS

Study design

This randomized, double-blinded, placebo-controlled trial was conducted at the Medical-Surgical Research Centre (Havana City, Cuba). The independent Institutional Ethics Committee approved the study protocol. Patients were enrolled after gave their informed written consent (visit 1), and at enrolment underwent physical examination and a complete medical history. Enrolled patients continued or started a five weeks baseline period on a step 1 cholesterol-lowering diet, after which their serum lipid profile was determined twice within 15 d . When blood sampling for the second determination was done, aliquots for assessing blood safety indicators were taken.

Eligible patients were randomized (visit 2) to receive ω-3-FA (1 g/d) + placebo or ω-3-FA (1 g/d) + policosanol 10 mg/d for 24 weeks and attended to further visits every 6 weeks. Patients underwent a physical examination at each visit, drug compliance and adverse experiences (AE) were controlled every 6 weeks and laboratory tests were done at baseline and at weeks 12 and 24.

Study participants

Men and women with documented hypercholesterolemia, aged 25 to 80 years, who attend usually to the lipid clinics, were enrolled in the trial.

Patients were excluded if they had active hepatic or renal diseases, diagnosed neoplastic diseases, uncontrolled hypertension (diastolic blood pressure ≥ 100 mmHg) or diabetes mellitus, or if had been hospitalized because any serious event within the three months prior to trial. Pregnant, nursing or women of childbearing potential without contraceptive protection were also excluded from the trial.

Causes of premature study discontinuations predefined included to have experienced any AE justifying such decision; unwillingness to follow-up, travels abroad, address changes, and major protocol violations (failure to consume study drugs for ≥ 10 consecutive days and /or consumption of lipid-lowering medications or supplements different from study drugs).

Treatment

Eligible patients were randomized to ω-3-FA-1 g capsules (batch 1586-02, Rainbow & Nature, Ltd., Sydney, Australia) administered together with placebo or policosanol (10 mg) tablets (Natural Products Plants, National Center for Scientific Research, Havana City, Cuba). The FA content of the ω-3-FA capsules (EPA 44.0 %, DHEA 37 %, with other n-3 FA at lower concentrations) was controlled through gas chromatography. Treatments were taken once a day with the evening meal for 24 weeks.

Patients were randomized according to a computer-generated code, using balanced blocks and 1/1 allocation

ratio, and received ω-3-FA in flasks, and policosanol or placebo tablets in identical coded packages.

The dose of ω-3-FA used in this trial was within those recommended for cardiovascular protection,[10-16] and that of policosanol dose was the highest assessed in the previous clinical studies of the effects of the combined therapy ω-3-FA-poli.[45,46]

Drug compliance was assessed through tablet and capsule counts and patients' interviews, being considered as good if they had consumed at least 85 % of the scheduled treatments, and good for the study if ≥ 80 % patients achieved such criterion. Compliance with diet was assessed though interview and body weight control.

The use of lipid-lowering treatments different from study drugs was not allowed during the study.

Efficacy variables

Serum LDL-C reduction was the primary efficacy variable. The effect of ω-3-FA-pla was considered as effective if compared with baseline it lowered LDL-C by at least 15 %,[47] and such reductions were significant compared with both baseline and ω-3-FA-pla. Other lipid profile markers were secondary efficacy variables.

Safety and tolerability

Data of physical (body weight, pulse rate, arterial pressure) and lab (alanine aminotransferase, aspartate aminotransferase, fasting glucose and creatinine) markers were analyzed.

An AE was defined as any undesirable experience occurred during the trial, independently if it was or not drug-related. According to their intensity, AE were classified as mild, moderate or serious. Mild AE did not require withdrawal of study drug or treatment of the AE, moderate AE required to stop drug intake and/or to treat the AE, and serious AE should lead to hospitalizations or deaths. AE were also ascertained as definitely, probably, possibly or doubtfully treatment-related using the Naranjo score.[48]

Laboratory analyses

Venous blood samples were drawn after 12 h overnight fasting. Serum TC and TG levels were determined through enzymatic methods using reagent kits (Roche, Basel, Switzerland), and HDL-C levels as per the cholesterol in the supernatant obtained after precipitating ß-lipoproteins.[49] LDL-C values were calculated with the Friedewald equation.[50] Blood safety indicators were determined with reagent kits from the same supplier, in a Hitachi 719 autoanalyzer (Tokyo, Japan) of the Medical Surgical Research Center.

Statistical analysis

Analyses were performed as per Intention-to-Treat. Hence, data of all randomized patients, as randomized, were included for the analyses, disregarding the degree of treatment compliance.

The sample size was calculated to detect, with 80 % power and $\alpha = 0.05$ a significant 20 % difference between the LDL-C reduction with ω-3-FA-poli compared with ω-3-FA-pla.

Within and between group differences of continuous data were compared with t test for paired and independent samples, respectively, and categorical data with the Fisher's Exact Probability Test. All statistical tests were two-tailed, with significance taken at $\alpha = 0.05$ and performed with the statistical software Statistics for Windows.

RESULTS

Baseline characteristics

Of the 63 patients enrolled, 60 (51 women, 9 men) were randomized, while three patients were not eligible because their baseline LDL-C values were below inclusion criteria. All randomized patients concluded the trial.

Both groups had well matched baseline characteristics (Table 1). The most frequent (> 20 %) risk factors observed in the study population were women older than 55 years, arterial hypertension, current smoking and family history of coronary disease. Many patients had multiple risk factors. Consumption of concomitant drugs was consistent with the risk factors of the patients.

Compliance with study treatments was good, since 55/60 (91.7 %) patients had good compliance, which was similar in both study groups.

Effects on lipid profile

The lipid profile values (Table 2) were similar in both groups at randomization. Treatment with ω-3-FA-pla did not change serum LDL-C at weeks 12 and 24, while ω-3-FA-poli reduced significantly ($p < 0.000\ 1$) such levels (by 23.4 % at week 12, by 26.0 % at week 24) compared with baseline and ω-3-FA-pla. At study completion, the frequency of patients with serum LDL-C reductions ≥ 15 % in ω-3-FA-poli (28/30, 93.3 %) group was significantly ($p < 0.001$) greater than ω-3-FA + placebo (1/30, 3.3 %).

After 12 and 24 weeks on treatment, ω-3-FA-poli also lowered significantly ($p < 0.000\ 1$) serum TC (15.4 and 16.6 %, respectively) and raised HDL-C (9.0 and 14.5 %) compared with ω-3-FA-pla, which unchanged these variables. Treatment with ω-3-FA-poli for 12 and 24 weeks reduced ($p < 0.000\ 1$) serum TG (by 16.7 and 23.3 %, respectively) *versus* baseline, but not *versus* -3-FA-pla, which lowered ($p < 0.000\ 1$ *versus* baseline) such values by 15.8 and 22.8 %, respectively.

Safety and tolerability

Both treatments were well tolerated. Except a mild, but significant reduction of serum aspartate aminotransferase values *versus* baseline in the ω-3-FA-poli group, no other significant differences of safety indicators were found, and individual values remained within normal limits (Table 3) (physical indicators values at weeks 6 and 18 not shown).

No patient withdrew from the trial. Seven patients (three in ω-3-FA-pla, four in ω-3-FA-poli) reported some mild AE: The ω-3-FA-pla patients referred dizziness (1) and acidity (2), while the ω-3-FA-poli patients reported headache (1), insomnia (1), acidity (1) and polyphagia (1). No between group differences were found. All the AE were considered as possibly drug-related.

DISCUSSION

This randomized, double-blind, study demonstrates that the combined therapy with ω-3-FA-poli administered for 24 weeks produced persistent benefits on the lipid profile of patients with hypercholesterolemia compared with ω-3-FA-pla. The present trial was conducted according to the approved protocol and the study population showed several coronary risk factors, being representative to that amenable to receive lipid-lowering therapy. All variables were well matched in both groups at baseline, which supports their homogeneity for assessing treatment effects and that the results here obtained should be attributable to the studied therapy.

After 12 and 24 weeks with ω-3-FA-poli LDL-C values, the primary efficacy variable, was reduced by 23.4 and

Table 1. Baseline characteristics of study patients.

Characteristics	Omega 3-FA + placebo (ω-3-FA-pla) (n = 30)	Omega 3-FA + policosanol (ω-3-FA-poli) (n = 30)
Age (years) (X ± SD)	64.6 ± 6.7	65.2 ± 6.5
Body mass index kg/m^2 (X ± SD)	25.4 ± 3.9	26.9 ± 4.9
	Gender n (%)	
Female	26 (86.7)	25 (83.3)
Male	4 (13.3)	5 (16.7)
	Coronary risk factors n (%)	
Women > 55 years	24 (80.0)	23 (76.7)
Hypertension	20 (66.7)	23 (76.7)
Men > 45 years	4 (13.3)	5 (16.7)
Current smoking	7 (23.3)	8 (26.7)
Obesity (kg/m^2 ≥ 30)	5 (16.7)	5 (16.7)
CHD	5 (16.7)	5 (16.7)
Diabetes mellitus	2 (6.7)	3 (10.0)
Family CHD	9 (30.0)	9 (30.0)
	Concomitant therapy[a]	
Diuretics	15 (50.0)	17 (56.7)
ACEI	8 (26.7)	9 (30.0)
β-blockers	9 (30.0)	8 (26.7)
Antiplatelets	9 (30.0)	7 (23.3)
Nitrates	4 (13.3)	4 (13.3)
Myorelaxants	4 (13.3)	3 (10.0)
Anxiolytics	3 (10.0)	3 (10.0)

CHD Coronary heart disease. ACEI Angiotensin converting enzyme inhibitors. AINE Anti-inflammatory non-steroidal drugs. [a] Consumed by at least three patients/group).

Table 2. Effects of policosanol, ω-3-FA and combined therapy on the lipid profile.

Groups	Baseline	12 weeks	% changes	24 weeks	% changes
		LDL-C (mmol/L)			
ω-3-FA-pla	4.39 ± 0.83	4.45 ± 0.84	+ 1.4	4.55 ± 0.78	+ 3.7
ω-3-FA-poli	4.28 ± 0.72	3.28 ± 0.62$^{****++++}$	23.4^{++++}	3.16 ± 0.51$^{****++++}$	26.0^{++++}
		Total cholesterol (TC) (mmol/L)			
ω-3-FA-pla	6.59 ± 0.98	6.52 ± 0.95	1.1	6.54 ± 0.86	0.8
ω-3-FA-poli	6.50 ± 0.80	5.50 ± 0.61$^{***++++}$	15.4^{+++}	5.41 ± 0.57$^{****++++}$	16.6^{++++}
		HDL-C (mmol/L)			
ω-3-FA-pla	1.40 ± 0.27	1.40 ± 0.28	0.0	1.37 ± 0.27^{+}	1.4
ω-3-FA-poli	1.45 ± 0.28	1.58 ± 0.29^{***++}	9.0^{++}	1.66 ± 0.26$^{****++++}$	14.5^{++++}
		Triglycerides (TG) (mmol/L)			
ω-3-FA-pla	2.15 ± 0.77	1.81 ± 0.57****	–15.8	1.66 ± 0.57****	–22.8
ω-3-FA-poli	2.10 ± 0.85	1.75 ± 0.56****	–16.7	1.61 ± 0.65****	–23.3

Results are expressed as (X ± SD). X Mean. DE Standard deviation.

* $p < 0.01$, ** $p < 0.001$, *** $p < 0.0001$ Comparison with baseline (t test for paired samples).

$^{+}$ $p < 0.05$; $^{++}$ $p < 0.01$, $^{+++}$ $p < 0.001$, $^{++++}$ $p < 0.000\ 1$ Comparison with placebo (t test for independent samples).

Table 3. Effects of policosanol, omega 3-FA and combined therapy on safety indicators of study patients.

Groups	Baseline	12 weeks	24 weeks
	Bodyweight (kg)		
ω-3-FA-pla	63.57 ± 11.31	63.67 ± 11.10	63.77 ± 11.57
ω-3-FA-poli	67.77 ± 13.03	67.82 ± 12.92	68.05 ± 12.73
	Pulse rate (beats/min)		
ω-3-FA-pla	68.70 ± 2.18	68.80 ± 1.00	69.23 ± 1.10
ω-3-FA-poli	69.73 ± 2.26	68.87 ± 1.01	69.53 ± 0.97
	Systolic blood pressure (mmHg)		
ω-3-FA-pla	129.67 ± 10.98	128.33 ± 9.50	128.00 ± 9.61
ω-3-FA-poli	131.33 ± 7.76	129.67 ± 7.65	129.00 ± 8.03
	Diastolic blood pressure (mmHg)		
ω-3-FA-pla	76.83 ± 6.50	77.33 ± 6.40	76.00 ± 5.63
ω-3-FA-poli	79.33 ± 5.83	78.67 ± 4.34	78.00 ± 4.84
	ALT (UI/L)		
ω-3-FA-pla	19.70 ± 8.19	21.10 ± 5.15	18.53 ± 7.40
ω-3-FA-poli	19.70 ± 8.11	20.60 ± 4.25	16.00 ± 5.07 **
	AST (UI/L)		
ω-3-FA-pla	23.03 ± 5.92	22.97 ± 4.99	25.73 ± 7.76
ω-3-FA-poli	22.47 ± 6.23	22.17 ± 3.34	24.60 ± 7.48
	Glucose (mmol/L)		
ω-3-FA-pla	5.06 ± 0.74	4.95 ± 0.60	5.35 ± 1.54
ω-3-FA-poli	5.08 ± 0.88	5.06 ± 0.70	4.89 ± 0.65
	Creatinine (μmol/L)		
ω-3-FA-pla	73.47 ± 24.27	75.93 ± 19.26	76.63 ± 21.88
ω-3-FA-poli	72.17 ± 22.33	75.83 ± 18.48	76.03 ± 21.24

Results are expressed as (X ± SD). X Mean. SD Standard deviation.

* $p < 0.05$ Comparison with baseline (t test for paired samples).

26.0 %, respectively, an effect significantly greater than that of ω-3-FA-pla, which indicates a persistent response. These LDL-C reductions are consistent with those (21.1 and 26.2 %) reported after 8 weeks of treatment with ω-3 -FA-poli (at 5 and 10 mg/d, respectively), in patients with hypercholesterolemia,[45] and somewhat greater than the reduction (17.4 %) obtained when such combined therapy was given for a shorter time (45 d).[46] In turn, the lack of effect of ω-3-FA + placebo on serum LDL-C was not surprising, since the effects of omega 3-FA alone on this variable have been controversial, modestly reducing, unchanging or raising such levels.[10-16]

Also, the frequency of patients achieving LDL-C reductions ≥ 15 % at the study completion (93.3 % with the combined therapy, 3.3 % with ω-3-FA-pla) indicates the benefit of administering ω-3-FA-poli compared with ω-3-FA-pla since LDL-C is the key surrogate for dyslipidemia management.

The other benefits of the combined therapy ω-3-FA-poli over ω-3-FA-pla, like the persistent serum TC decrease and HDL-C increase, are consistent with previous results.[45,46] Also, although ω-3-FA-poli did not improve the TG-lowering effect of ω-3-FA-pla, it did not impair such response.

In addition, the effects of the combined therapy ω-3-FA-poli match well the mechanism of action of both drugs. Thus, the cholesterol lowering effect of policosanol is linked with the inhibition cholesterol synthesis through the regulation of the activity of the hidroxymethylglutaryl coenzyme A reductase (HMGCoA) enzyme mediated by the activation of AMP kinase,[51-54] and with the increase of LDL-receptor processing, which leads to the reduction of serum LDL-C.[51-53]

In turn, ω-3-FA reduces the synthesis and secretion of very-low-density lipoprotein (VLDL) particles, and increase TG removal from VLDL and chylomicron particles through the up-regulation of enzymes, like lipoprotein lipase.[14,55-57] Since policosanol differs mechanistically from the effect of -3-FA it can be understood why it can add complementary lipid benefits when administered together with ω-3-FA.

According to its design, however, this study does not allow conclude the benefits of ω-3-FA-poli versus ω-3 -FA-pla, since it did not include a policosanol + placebo group. Nevertheless, the reductions of LDL-C and TC, and the increase of HDL-C here shown are consistent with the policosanol effects found in most of the clinical trials conducted in Cuba and abroad.[20-41]

Finally, consistently with previous results,[45,46] the treatments were well tolerated. No patient discontinued from the study, safety indicators were unaffected and AE were mild and similar in both groups.

CONCLUSIONS

Combined therapy with ω-3-FA-poli given for 24 weeks lowered LDL-C, TC, raised HDL-C, and unaffected TG compared ω-3-FA + placebo, and was well tolerated by hypercholesterolemic patients. These results merit that further studies investigate the effects of this combined therapy administered longer and comparing its benefits compared with policosanol monotherapy.

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