Research Article

Policosanol versus Atorvastatin on the Functional Recovery of Patients with Ischemic Stroke

Javier Sánchez,[1] José Illnait,[2] Rosa Mas,[3] Sarahí Mendoza*,[3] Hermys Vega,[2] Lilia Fernández,[3] BsC Meilis Mesa,[2] Julio Fernández,[3] Eng. Pablo Reyes,[4] Eng Dalmer Ruiz[4]
[1]Institute of Neurology and Neurosurgery, Havana, Cuba.
[2]Surgical Medical Research Centre, Havana, Cuba.
[3]Center of Natural Products, Havana, Cuba.
[4]Database branch, National Center for Scientific Research, Havana, Cuba.
***Corresponding author's E-mail:** sarahi.mendoza@cnic.edu.cu

Accepted on: 13-06-2015; **Finalized on:** 29-02-2016.

ABSTRACT

Stroke is among the leading causes of mortality and disability. Statin may improve stroke functional outcome. Policosanol added to aspirin (AS) therapy improves stroke outcome compared to placebo + AS. The objective is to compare the efficacy of policosanol and atorvastatin on the functional stroke in patients who had had a recent ischemic stroke. Patients who had suffered a recent (≤ 30 days evolution) stroke and had modified Rankin Scale scores (mRSs) between 2 and 4 were double-blindly randomized to policosanol (20 mg/day) or atorvastatin (20 mg/day) for 12 weeks. The primary outcome was the reduction of mRSs at 12 weeks after randomization, and the secondary outcome the increase of the Barthel Index (BI). Sixty patients (mean age: 68 years) were randomized, and all completed the study. After 4 weeks on therapy, both treatments decreased significantly ($p<0.001$) mean mRSs versus baseline. This effect improved thereafter, achieving decreases of 56.5% (policosanol) and 52.2% (atorvastatin), respectively, at study completion. No significant differences between groups were seen. BI increased significantly ($p<0.00001$) in both groups at week 4 and such effect was enhanced thereafter. The increase with policosanol was higher ($p<0.01$) than with atorvastatin. Low-density lipoprotein-cholesterol (LDL-C) and total cholesterol (TC) decreased significantly with both treatments, but more ($p<0.05$ and $p<0.01$, respectively) with atorvastatin. HDL-C increased significantly ($p<0.01$) with policosanol, not with atorvastatin. Triglycerides remained unchanged in both groups. Policosanol (20 mg/day) and atorvastatin (20 mg/day), administered for 12 weeks within the next 30 days after stroke onset, were similarly effective for improving the functional outcome in ischemic stroke patients treated with AS.

Keywords: aspirin, atorvastatin, ischemic stroke, policosanol, Rankin-modified scale, Barthel Index.

INTRODUCTION

Stroke, which results from the sudden interruption of blood flow to a brain region that impairs the energy supply to the central nervous system, may be ischemic (75-80% of cases) or haemorrhagic (about 20%).[1] Hypoxia is the main cause of central nervous system damage in stroke. Although neurons and glial cells have functional changes in the penumbra, neurons are more vulnerable to hypoxia because they depend on the oxidative metabolism of glucose for energy.[2]

Ischemic stroke is among the leading causes of mortality and disability worldwide. About half of stroke survivors remain with physical or cognitive impairment that affect their physical function, social function and daily activities. Also, stroke implies a high cost to patients, families and health systems.[3,4] Control of modifiable stroke risk factors, such as hypertension, diabetes, dyslipidemia, cigarette smoking and obesity are key measures to prevent recurrent strokes.[5] Currently it is accepted that control of low-density lipoprotein-cholesterol (LDL-C) levels is relevant for stroke prevention, mainly among subjects with cardiovascular disease.[6]

Statins lower the stroke risk in different population subsets,[7-9] including subjects without history of established cardiovascular disease.[10] Greater reductions in stroke are associated with higher LDL-C decreases.[11] Across all populations, statins were more effective than placebo in lowering the risk of non-fatal, but not of fatal strokes, without differences among different statins, such as atorvastatin, pravastatin and simvastatin.[12]

Pre-treatment with statins has shown to lower infarct sizes and to improve functional outcomes in experimental stroke.[13] Clinical studies, however, have provided conflicting effects of statins on stroke functional outcomes.[14-19] Statin pre-treatment has been associated with favourable outcomes in acute ischemic stroke,[14] but not all studies agree with that. Pre-treatment with statins did not decrease stroke severity and did not improve 30-day survival in older patients who suffered ischemic stroke. However, both the 12-month survival and the 12-month functional outcome (evaluated through the modified Rankin Scale score – mRSs-) were significantly better in the group treated with statins after stroke.[15] Likewise, while statin use during hospitalization has shown to improve the clinical outcomes of acute first-ever minor ischemic strokes,[16] recent data demonstrated that pre-stroke or early-stroke statin therapy did not reduce the infarct volume, or improve clinical or functional outcome at 3 months in patients with minor strokes.[17] In a large meta-analysis that included data of 113000 patients, statin therapy at stroke onset was

associated with improved outcome.[18] See comment in PubMed Commons below.

Policosanol, a mixture of 8 high molecular weight sugarcane wax alcohols, has been shown protective effects in experimental brain ischemia,[19-21] and clinical studies have found coherent results.[22-25] Long-term (5 years) open studies found that policosanol added to AS therapy was associated to a very good neurological recovery.[22,23] Likewise, two double-blind, placebo-controlled studies demonstrated that policosanol 20 mg/day + aspirin (AS) administered for 6 months improved the neurological recovery as compared to placebo + AS in patients with recent (≤30 days) ischemic stroke.[24,25]

In light of these issues, this study compared the effects of policosanol (20 mg/day) and atorvastatin (20 mg/day) on the functional outcome in patients who had had a recent ischemic stroke, all treated with AS from their admission in the stroke emergency unit.

MATERIALS AND METHODS

Study design

This study was conducted in the Institute of Neurology and Neurosurgery (Havana, Cuba) after being approved by the Institutional Ethics Committee. The study enrolled patients who had had recent ischemic stroke within the 30 days before recruitment and have provided their informed written consent (Visit 1). Participants underwent clinical history and full clinical examination, and were advised to start or continue on a low-sodium and low fat diet. Smokers were strongly encouraged to stop smoking.

Eligible patients were double-blinded randomized to policosanol or atorvastatin (visit 2) for 12 weeks and attended to control visits at 4, 8 and 12 weeks on treatment (visits 3–5). Patients underwent general examination and neurological assessment at each visit. Treatment compliance and adverse experiences (AE) were controlled from visits 3 to 5, and laboratory analyses at baseline and after 12 weeks on treatment.

Study patients

Participants were men and women over 40 years of age who had had an ischemic stroke within the 30 days prior to enrolment. Stroke was defined as the occurrence of focal clinical signs of central nervous system dysfunction of vascular origin that lasted for at least 24 hours. Ischemic stroke was confirmed through clinical assessment and tomography scan conducted within the 48 hours after stroke onset.

Eligible patients fulfilled the enrolment criteria and had mRSs of 2, 3 or 4 (2–4).[26]

Exclusion criteria were to have had haemorrhagic stroke, atrial fibrillation, other cardiac sources of embolism, subarachnoid haemorrhage, diastolic hypertension ≥ 110 mm Hg, cardiac valve diseases, history of myocardial infarction, instable angina or revacularisation surgery within the 6 months prior to the trial and previous consumption of policosanol.

Treatment

Patients consumed policosanol or atorvastatin (20 mg tablets for both) once daily with the breakfast for 12 weeks. Policosanol and atorvastatin tablets were produced in MedSol and NOVATEC (Havana, Cuba), respectively. To ensure the double-blind allocation to treatments without affecting their respective formulations, a double-dummy method was used. Policosanol patients received one policosanol 20 mg + one atorvastatin placebo tablet, and atorvastatin patients received one atorvastatin 20 mg + one policosanol placebo tablet.

Because the risk of stroke recurrence peaks in the first few hours/days after stoke onset, AS was commenced early after admission in the stroke emergency unit. The AS dose (125 mg/day) was selected keeping in mind that daily doses between 75 and 150 mg are recommended for the prevention of vascular events in high-risk patients, without increased risk of haemorrhagic events.[27-29]

Good treatment compliance, assessed through counts of remainder tablets and patient's interviews, was to consume at least 85% of scheduled tablets per period.

The consumption of cholesterol-lowering or antiplatelet drugs was prohibited during the study. Likewise, patients who were taking these medications had to stop them 30 days before to enrolment.

Study outcomes

Clinical response was defined in terms of two stroke functional scales: the mRSs and the Barthel Index (BI), which measure patient disability.[26,30]

The primary outcome of this study was functional outcome measured by the mRSs at 12 weeks after randomization. We assumed that the treatments should produce a comparable reduction of the mRSs at 12 weeks and significant versus baseline.

The mRSs assesses functional stroke outcome with scores that range from 0 to 6 (0 no symptoms; 1 no relevant disability despite symptoms, able to conduct all usual activities; 2 slight disability, unable to carry out all previous activities but able to conduct self-assistance; 3 moderate disability requiring some help, but able to walk without assistance; 4 moderate severe disability, unable to walk without assistance, and unable to attend body needs without assistance; 5 serious disability; bedridden, incontinent, and requiring constant care and attention; and 6 death).[26]

The secondary outcome of the trial was functional outcome measured by the increase on the BI at 12 weeks after randomization. BI assesses patient independence in daily activities with a score that ranges from severe dependence to no disability.[30,31] Each item is rated on this

scale with a number of points assigned to each ranking. The scales uses ten variables to describe mobility, feeding, toilet use, dressing, bathing, faecal and urinary incontinence, the help needed with grooming and other activities. A higher number is associated with a greater degree of independence following discharge from hospital. Each item can score 0, 5 or 10 points, so that BI ranges from 0 to 100, corresponding to six levels of dependence: independent (100 points), low dependence (91–99 points), moderate dependence (61–90 points), severe dependence (41–60 points), moderate dependence (21-40) and total dependence (0–20).[31,32]

A value of mRSs≤ 1 and a BI score of 95 to 100 at 12 weeks were considered as favourable outcomes.[14,18]

Decreases on lipid LDL-C, total cholesterol (TC) and triglycerides (TG), as well as increases on high-density lipoprotein-cholesterol (HDL-C) levels were collateral efficacy variables.

Laboratory analyses

Venous blood samples were taken following a fasting of 12 hours. Serum was separated by centrifugation at 4°C and 2000 x *g* for 10 min, and aliquots were immediately taken. Lab analyses were performed within the next 8 hours after blood drawing.

Lipid profile and blood safety indicators

Serum levels of TC, TG, HDL-C and blood biochemistry indicators were determined using reagent kits (Roche, Basel, Switzerland) in a Hitachi 719 autoanalyzer (Tokyo, Japan) of the clinical laboratory of the Medical Surgical Research Centre. LDL-C values were calculated by using the Friedewald equation.[32]

Safety and tolerability assessment

Safety and tolerability indicators included laboratory and physical examination data, and AE reports. Study protocol defined an AE as any undesirable experience, absent at hospital discharge or worsened thereafter, happening in a patient, independently if it could be or not related with the therapy. AE were classified as mild, moderate or serious according to their intensity. Mild AE should not require stopping of study medications or specific treatment of the AE, moderate AE should require the withdrawal of study medications and/or treatment of the AE, while serious AE should lead to patient hospitalization and/or to death.

Statistical Analysis

The study was designed to have a statistical power of 80% and a two-sided significance level of $p<0.05$ to detect a significant reduction of the mean mRSS as compared to baseline, without difference between the groups.

Given the specified statistical power, we needed 60 eligible patients. Assuming a total dropout rate of 10%, we should enrol at least 66 patients.

Data were analysed on an intention-to-treat basis, including those of all patients who underwent randomization. Analysis of Variance was used for repeated comparisons of continuous variables (mean mRSS values, bodyweight, pulse rate, arterial pressure). Laboratory variables were compared using the Wilcoxon test for paired matched samples (within group comparisons) and the Mann Whitney U test (between group comparisons). Categorical data were compared with the Fisher Exact probability test. All p values were two-sided.

RESULTS

Population characteristics

Of 70 screened patients, 60 (mean age: 68 years) (24 men, 36 women) were eligible for randomization. All randomized patients (100%) completed the trial.

Baseline characteristics were well matched in both groups (Table 1). The most frequent (≥20%) risk factors at baseline were sedentary life (100%), salt-rich diet (100%), hypertension (98.3%), overweight plus obesity (76.7%) smoking (56.7%), and diabetes (21.7%). Concomitant therapy was also well balanced in the two groups, the most frequent being the angiotensin converting enzyme inhibitors (ACEI) (93.3%).

Effects on stroke functional outcomes

During the study drug compliance was ≥90% and similar in both groups. No patient had recurrent cerebrovascular event or any other major vascular event during the trial.

The baseline distribution of patients into the different mRSs values (Table 2) was similar in both groups. After 12 weeks on therapy, the frequency of policosanol patients (30/30, 100%) who achieved mRSs ≤1 was comparable to that in the atorvastatin group (27/30, 90%).

Table 3 summarizes the effects on both functional stroke scales. After 4 weeks on therapy, policosanol and atorvastatin decreased significantly ($p<0.001$) mRSs values versus baseline, and this treatment effect did not wear off, but improved thereafter, so that significant decreases of 56.5% and 52.2%, respectively, were found at study completion. No significant between group differences were seen.

Baseline values of the BI were also well balanced in the two groups (Table 3). After 4 weeks on therapy, both treatments increased significantly ($p<0.00001$) the BI versus baseline, and this effect was enhanced thereafter, so that increases of 16.5% (policosanol) and 13.4% (atorvastatin) were obtained at study completion. At weeks 4 and 8 policosanol increased the BI ($p<0.05$ and $p<0.01$, respectively) more than atorvastatin (Table 3). At week 12, the frequency of policosanol (30/30, 100 %) and atorvastatin (28/30, 93.3%). Patients who achieved BI scores ≥ 90 was comparable.

Effects on lipid profile

All lipid variables were statistically similar at randomization. LDL-C and TC decreased significantly with policosanol (17.8% and 9.7%, respectively) and with atorvastatin (31.1% and 21.7%, respectively) ($p<0.01$ vs baseline with policosanol, $p<0.001$ vs baseline with atorvastatin) (Table 4). The reductions achieved with atorva + AS were significantly higher than those of policosanol ($p<0.01$). HDL-C increased significantly (12.6%) with poli + AS ($p<0.05$ vs baseline), but did not change significantly with atorvastatin. The two treatments failed to modify TG levels.

Table 1: Baseline characteristics of study population

Characteristics	Poli + AS (n=30)	Atorva + AS (n=30)	Total (n=60)
Age (years) (X ± SD)	69 ± 9	67 ± 11	68 ± 10
Body mass index (kg/m^2) (X ± SD)	26.2 ± 1.5	26.0 ± 1.4	26.0 ± 1.5
Women n (%)	19 (63.3%)	17 (56.7%)	36 (60.0%)
Men n (%)	11 (36.7%)	13 (43.3%)	24 (40.0%)
mRSs (X ± SD)	2.30 ± 0.47	2.30 ± 0.47	2.30 ± 0.47
Salt-rich diet (n)	30 (100%)	30 (100%)	60 (100%)
Sedentary life (n)	30 (100%)	30 (100%)	60 (100%)
Hypertension (n)	29 (96.7%)	30 (100%)	59 (98.3)
Overweight & obesity (n)	25 (83.3%)	21 (70%)	46 (76.7%)
Smoking (n)	19 (63.3%)	15 (50.0%)	34 (56.7)
Diabetes (n)	8 (26.7%)	5 (16.7%)	13 (21.7%)
Hypercholesterolemia (n)	6 (20.0%)	5 (16.7%)	11 (18.3%)
Concomitant therapy (≥5%)			
Consumers of at least 1 concomitant therapy	29 (96.7%)	30 (100.0%)	59 (98.3%)
ACEI	29(96.7%)	27 (90.0%)	56 (93.3%)
Diuretics	3 (10.0%)	5 (16.7%)	8 (26.7%)
Oral hypoglycemic drugs	4 (13.3%)	3 (10.0%)	7 (23.3%)

(X ± SD) mean ± standard deviation. Poli policosanol, Atorva atorvastatin, mRSs Modified Ranking Scale score, ACEI angiotensing converting enzyme inhibitors; All comparisons were not significant

Table 2: Distribution of cases in accordance to the Modified Ranking Scale score (mRSs)

mRSs values	Baseline		12 weeks	
	Poli + AS	Atorva + AS	Poli + AS	Atorva + AS
0	0	0	0	0
1	0	0	30	27
0–1	0	0	30	27
2–3	30	30	0	3
4	0	0	0	0

Data presented as n (number of cases), Poli policosanol, Atorva atorvastatin, AS aspirin; (Fischer´s Exact Probabilty test)

Table 3: Effects on neurological recovery assessed through the functional stroke scales

Treatment	Baseline	4 weeks	8 weeks	12 weeks	% change vs baseline
Modified Rankin Scale score (mRSs) (X ± SD)					
Poli + AS	2.30 ± 0.47	1.57 ± 0.50**	1.10 ± 0.30***	1.00 ± 0.00***	**-56.5**
Atorva + AS	2.30 ± 0.47	1.73 ± 0.45*	1.20 ± 0.41***	1.10 ± 0.30***	**-52.2**
Barthel Index (BI) (X ± SD)					
Poli + AS	79.83 ± 2.78	87.33 ± 3.41***	91.83 ± 3.34^{***+}	93.00 ± 2.49^{***++}	**+16.5**
Atorva + AS	79.83 ± 3.07	86.00 ± 3.81***	89.83 ± 3.34***	90.50 ± 3.04***	**+13.4**

(X ± SD) mean ± standard deviation. Poli policosanol, Atorva atorvastatin, AS aspirin; $^{*}p<0.001$, $^{**}p<0.0001$, $^{***}p<0.00001$ (Wilcoxon test for matched samples, Bonferroni adjustment); $^{+}p<0.05$, $^{++}p<0.01$ Comparison with Atorva + AS (Mann Whitney U test)

Table 4: Effects on lipid profile (mmol/L) (X ± SD)

Treatment	Baseline	12 weeks	% changes from baseline
Low-density lipoprotein-cholesterol (LDL-C)			
Poli + AS	4.04 ± 0.68	3.32 ± 1.14**	**-17.8**
Atorva + AS	3.89 ± 0.97	2.68 ± 0.90***+	**-31.1**
Total cholesterol (TC)			
Poli + AS	5.77 ± 0.82	5.21 ± 1.16**	**-9.7**
Atorva + AS	5.57 ± 1.10	4.36 ± 1.14***++	**-21.7**
High-density lipoprotein-cholesterol (HDL-C)			
Poli + AS	1.19 ± 0.35	1.34 ± 0.44*	**+12.6**
Atorva + AS	1.17 ± 0.53	1.19 ± 048	**+1.7**
Triglycerides			
Poli + AS	1.60 ± 0.93	1.48 ± 0.76	**-7.5**
Atorva + AS	1.40 ± 0.53	1.31 ± 0.61	**-6.4**

X mean, SD standard deviation, Poli policosanol, Atorva atorvastatin, AS aspirin; *p<0.05, **p<0.01,***p<0.001, Comparisons with baseline (Wilcoxon test for matched samples); + p<0.05, ++ p<0.01 Comparison with Atorva + AS (Mann Whitney U test)

Safety and tolerability

Treatments were safe and well tolerated. No patient discontinued from the study. Treatments did not impair safety physical or blood indicators and individual values were not out of normal limits (data not shown for simplicity).

Eight patients, all atorvastatin-treated, experienced AE during the study: 4 referred muscle pain, 4 experienced heartburn and 1 reported to have stomach pain, without significant differences between the groups.

DISCUSSION

The aim of the present study was to compare the effects of policosanol (20 mg/day) and atorvastatin (20 mg/day) added to the conventional AS therapy on the functional outcome of patients who had had a recent ischemic stroke of moderate severity. There were no differences between the treatment groups on the reduction of the mRSs versus baseline, primary outcome of the study, then the efficacy of policosanol and atorvastatin on the stroke functional outcome was shown to be comparable.

Study patients were randomized within 30 days of the onset of the ischemic stroke, so that the effects of policosanol and atorvastatin here seen cannot be interpreted as proofs of the treatments on the acute stroke, but on the further recovery step. Following the recommendations for ischemic stroke management, all patients received AS early on their admission in stroke unit and followed on this thereafter.[27-29]

The strength of this study include that it was randomized, double-blinded and controlled with a group that received atorvastatin, a statin with well documented benefits on stroke patients. Evidence support that continuation or starting statins, mainly atorvastatin, after ischemic stroke may reduce mortality and improve outcome.[33,34] Study patients, however, had not been received statins or policosanol before being randomized, so that they were technically virgin to study treatments. Our eligible study population was restricted to have 2 to 4 mRSs values for lowering the influence of the variability of stroke severity on the results.

Since both groups were homogeneous at baseline the effects here observed can be attributable to the respective treatments. In particular, the mean mRSs and BI values were comparable in the two study groups. In addition, See comment in PubMed Commons below the fact that all randomized patients (100%) concluded the study and that treatment compliance was very good (>90%) and comparable in both groups supports the validity of the present results.

Baseline characteristics of study population match well with stroke epidemiological data. The mean age of patients, and the high frequency of concomitant morbidities were consistent with common stroke risk factors. In addition to AS, consumed by all patients, the most frequent concomitant medications were ACEI, but such consumption, coherent with the prevalence of hypertension well balanced in both groups, was also similar in the two groups, so that we discard the potential influence of concomitant therapy to the present results.

Stroke scales, developed for assessing the degree of patient recovery and the need of standardization for comparing the data across the studies, have been used as primary or secondary outcomes for evaluating the neurological improvement in stroke studies.[35,36] We assessed the effects on stroke outcome by measuring the functional status and degree of functional dependence of

the patients with the mRSs and the BI at randomization, 4 weeks, 8 weeks and 12 weeks after treatment. Indeed, the mRSs and BI are widely used functional impairment and disability scales, and in particular, mRS has been that most widely used clinical outcome tool for stroke recovery in clinical studies.[33,35-38]

The present results support confirms that the addition of policosanol to conventional AS therapy after hospital discharge should help the neurological recovery post-ischemic ischemic stroke assessed through the mRSs, the primary study outcome. This asseveration is based on the mean reduction of mRSs (- 56.5%) in the policosanol group, and on the proportion of patiens who achieved a good stroke outcome (mRSs ≤1)(30/30, 100%) at study completion. These results are consistent with the efficacy of policosanol on previous randomized, double-blind controlled studies in which the control group received placebo + AS. The decrease of the mean mRSs here seen at week 12, however, was higher than those achieved at week 12 post-stroke in such previous placebo controlled studies (31% and 39.0%), and the same happens for the rate of patients who achieved mRSss values ≤1) (10/46, 21.74 % and 11/31, 35.48 %).

Also, and the most relevant is that this study demonstrates, by the first time, that the efficacy of policosanol added to conventional AS therapy as soon as one month after stroke, was similar to that of atorvastatin (20 mg/day) added to AS treatment in same conditions. So, the values of mean reduction of mRSs (-52.2%) with atorvastatin, and the rate of patients who reached a good stroke outcome (27/30, 90%) were statistically similar to those achieved with policosanol. Despite there are relatively few data on the effects of atorvastatin on mRSs values, the usefulness of statins on ischemic stroke recovery makes the present comparison as valid. Also, keeping in mind the neurological improvement at 12 weeks after stroke in the NINDS rt-PA study (11-13% reduction of mRSs) despite the patients were treated as soon as within the first hours of acute stroke,[24] we should consider that the results achieved with policosanol and atrovastatin were clinically meaningful.

There were not recurrent strokes or ischemic transient attacks among study participants, a result particularly good since the highest probability of recurrent events occurs within the first 12 weeks post-stroke.[4,5] This result confirms the usefulness of the therapies in patients who had experienced an ischemic stroke.

In line with the results obtained on the mRSs, both treatments improve the neurological response evaluated through the BI. In this case, policosanol and atorvastatin increased significantly the BI versus baseline. Different from the results obtained in the assessment with mRSs, the neurological response to policosanol assessed through BI was better than that of atorvastatin. Nevertheless, the final BI values and the rate of patients that achieved a BI score of 95 to 100 in both groups support a very good neurological recovery, which limits the relevance of this advantage of policosanol, at least in this study. As compared to mRSs, the BI assesses actual performance of activities of daily living (ADL) and among the ADL measures, the BI is that most used to assess stroke patients' actual performance on ADL functions in clinical routine and clinical studies, as well.[30,31,35,37,38]

Despite both treatments reduced significantly LDL-C and TC, atorvastatin was most effective for lowering LDL-C (31.1%) and TC (21.7%), as expected. Policosanol was effective for lowering LDL-C (17.8%) and TC (9.7%). The reductions here seen, however, are lower than in previous studies conducted in stroke patients,[24,25] a result for which we have not conclusive explanation. Although some report have failed to find lipid/lowering effects of other policosanol tablets,[39–41] several trials support the cholesterol-lowering effects of policosanol.[42-48] On its side, HDL-C increased with policosanol, not with atorvastatin. This effect of policosanol should be favourable for post-stroke patients due to the association between increasing HDL-C and stroke prevention.[49] Nevertheless, the lack of between group significance prevents limits say that this effect is an advantage of policosanol over atorvastatin for patients who had suffered an ischemic stroke.

Consistent with previous studies, policosanol and atorvastatin were safe and well tolerated. No treatment impaired the safety indicators, none discontinued the study due to AE, and all AE were mild.

The frequency of patients who experienced AE (none policosanol, eight atorvastatin treated) seems to favour policosanol, was the difference was not statistically significant.

CONCLUSION

Policosanol (20 mg/day) and atorvastatin (20 mg/day), administered for 12 weeks within the next 30 days after stroke onset, were similarly effective for improving the functional outcome in patients with recent ischemic stroke, all treated with AS.

Acknowledgement: A research grant of the National Centre for Scientific Research supported the conduction of this study. No financial interests influence the conclusions or outcome of this study report. No author has received financial support from a commercial source.

REFERENCES

1. Amarenco P, Bogousslavsky J, Caplan LR, Donnan GA, Hennerici MG, Classification of stroke subtypes, Cerebrovasc Dis, 27, 2009, 493-501.
2. Amantea D, Nappi G, Bernardi G, Bagetta G, Corasaniti MT, Post-ischemic brain damage: pathophysiology and role of inflammatory mediators, Febs J, 276, 2009, 13–26.
3. Di Carlo A, Human and economic burden of stroke, Age Ageing, 38, 2009, 4-5.

4. Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, Borden WB, Heart disease and stroke statistics—2012 update, Circulation, 125, 2012, e2-220.
5. Couillard P, Poppe AY, Coutts SB, Predicting recurrent stroke after minor stroke and transient ischemic attack, Expert Rev Cardiovasc Ther, 7, 2009, 1273–1281.
6. Arboix A, Cardiovascular risk factors for acute stroke: Risk profiles in the different subtypes of ischemic stroke World J Clin Cases, 3, 2015, 418-29.
7. Amarenco P, Labreuche J, Lipid management in the prevention of stroke: review and updated meta-analysis of statins for stroke prevention, Lancet Neurol, 8, 2009, 453-63.
8. O'Regan C, Wu P, Arora P, Perri D, Mills EJ, Statin therapy in stroke prevention: a meta-analysis involving 121,000 patients, Am J Med, 121, 2008, 24-33.
9. Filalo J, Duque G, Steele R, Jukema W, de Craen AJ, Eisenberg MJ, Statins for secondary prevention in elderly patients: a hierarchical bayesian meta-analysis, J Am Coll Cardiol, 51, 2008, 37-45.
10. Kearney PM, Blackwell L, Collins R, Keech A, Simes J, Peto R, Efficacy of cholesterol-lowering therapy in 18,686 people with diabetes in 14 randomised trials of statins: a meta-analysis, Lancet, 371, 2008, 117-125.
11. Rugts JJ, Yetgin T, Hoeks SE, Gotto AM, Shepherd J, Westendorp RG, The benefits of statins in people without established cardiovascular disease but with cardiovascular risk factors: meta-analysis of randomised controlled trials, BMJ, 2009, 338, b2376.
12. Naci H, Brugts JJ, Fleurence R, Ades AE, Comparative effects of statins on major cerebrovascular events: a multiple-treatments meta-analysis of placebo-controlled and active-comparator trials, QJM, 106, 2013, 299-306.
13. Guan W, Kozak A, Fagan SC, Drug repurposing for vascular protection after acute ischemic stroke, Acta Neurochir Suppl, 111, 2011, 295-298.
14. Lakhan SE, Bagchi S, Hofer M, Statins and clinical outcome of acute ischemic stroke: a systematic review, Int Arch Med, 3, 2010, 3, 22.
15. Hjalmarsson C, Bokemark L, Manhem K, Mehlig K, Andersson B, The effect of statins on acute and long-term outcome after ischemic stroke in the elderly, Am J Geriatr Pharmacother, 10, 2012, 313-322.
16. Song B, Wang Y, Zhao X, Liu L, Wang C, Wang A, Association between statin use and short-term outcome based on severity of ischemic stroke: a cohort study, PLoS One, 9, 2014, e84389.
17. Asdaghi N, Coulter JI, Modi J, Camden MC, Qazi A, Goyal M, Statin therapy does not affect the radiographic and clinical profile of patients with TIA and minor stroke, Am J Neuroradiol, 2015, Apr 23 [Epub ahead of print].
18. Chróinín N, Asplund K, Asberg S, Callaly E, Cuadrado E, Díez E, Statin therapy and outcome after ischemic stroke: systematic review and meta-analysis of observational studies and randomized trials, Stroke, 44, 2013, 448–456.
19. Arruzazabala ML, Carbajal D, Molina V, Valdés S, Mas R, Effect of policosanol on cerebral ischemia in Mongolian gerbils: Role of prostacyclin and thromboxane A2, Prostag, Leuk and Ess Fatty Acids, 49, 1993, 695-697.
20. Molina V, Arruzazabala ML, Carbajal D, Valdés S, Noa M, Mas R, Effect of policosanol on cerebral ischemia in Mongolian gerbils, Brazil J Med Biol Res, 32, 1999, 1269-1276.
21. Molina V, Ravelo Y, Noa M, Mas R, Pérez Y, Oyarzábal A, Therapeutic Effects of Policosanol and Atorvastatin against Global Brain Ischaemia-Reperfusion Injury in Gerbils, Indian J Pharm Sci, 75, 2013, 635-641.
22. Ortega L, Sánchez J, Mas R, Fernández L, Mendoza S, Gamez R, Effects of policosanol on patients with ischemic stroke. A pilot open study, J med food, 9, 2006, 378–385.
23. Sanchez J, Mas R, Mendoza S, Fernández J, Ruiz D, Effects of policosanol on patients with ischemic stroke with previous transient ischemic attack: a long-term follow-up, Rev CENIC Cien Biol, 41, 2010, 41, 23-29.
24. Sánchez J, Fernández L, Illnait J, Arruzazabala ML, Molina V, Mas R, Effects of policosanol on the recovery of ischemic stroke: a randomized controlled study, IOSR Journal of Pharmacy, 2, 2012, 14-24.
25. Sánchez J, Fernández L, Illnait J, Arruzazabala ML, Molina V, Mas R, Effects of policosanol on the recovery of ischemic stroke: a randomized controlled study. IOSR Journal of Pharmacy, 4, 2013, 31-40.
26. Rankin J. Cerebral vascular accidents in patients over the age of 60. II. Prognosis, Scott Med J, 2, 1957, 200-215.
27. Antithrombotic Trialists' Collaboration, Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction and stroke in high/risk patients, BMJ, 324, 2000, 71–86.
28. Levi M, Thromboprophylaxis for cerebrovascular disorders: acetylsalicylic acid remains the cornerstone, Ned Tijdschr Geneeskd, 152, 2008, 423-425.
29. Likosky DJ, Lee K, Brown DM, Amin A, Dressler DD, Krakow D, Evidence-based medicine: Review of guidelines and trials in the prevention of secondary stroke, J Hosp Med, 3, 2008, S6-S19.
30. Mahoney FI, Barthel DW, Functional evaluation: the Barthel index, Md Med J, 14, 1965, 61–65.
31. Quinn TJ, Langhorne P, Stott DJ, Barthel index for stroke trials: development, properties, and application, Stroke, 42, 2011, 1146–1151.
32. Friedewald WT, Levy RI, Fredrickson DS, Estimation of the concentration of low density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge, Clin Chem, 18, 1972, 499-502.
33. Miedema I, Uyttenboogaart M, Koopman K, De Keyser J, Luijckx GJ, Statin use and functional outcome after tissue plasminogen activator treatment in acute ischaemic stroke, Cerebrovasc Dis, 29, 2010, 263-267.
34. Fisher M, Moonis M, Neuroprotective effects of statins: evidence from preclinical and clinical studies, Curr Treat Options Cardiovasc Med, 14, 2012, 252-259.
35. Ghandehari K, Challenging comparison of stroke scales, J Res Med Sci, 18, 2013, 906–910.

36. The National Institute for Neurological Desorders and Stroke rt-PA Stroke Study Group, N Engl J Med, 333, 1995, 1581-1587.

37. Lee YC, Chen SS, Koh CL, Hsueh IP, Yao KP, Hsieh CL, Development of two Barthel Index-based Supplementary Scales for patients with stroke, PLoS One, 9, 2014, e110494.

38. Mar J, Masjuan J, Oliva J, Gonzalez N, Becerra V, Casado M, Outcomes measured by mortality rates, quality of life and degree of autonomy in the first year in stroke units in Spain, Health Qual Life Outcomes, 13, 2015, 36.

39. Berthold HK, Unverdoben S, Degenhardt R, Bulitta M, Gouni-Berthold I, Effect of policosanol on lipid levels among patients with hypercholesterolemia or combined hyperlipidemia: a randomized controlled trial, JAMA, 295, 2006, 2262–2269.

40. Francini F, Beltramolli D, Dall´acqua S, Brocadello F, Effect of sugar cane policosanol on lipid profile in primary hypercholesterolemia, Phytother Res, 22, 2008, 318–322.

41. Mas R, Castaño G, Illnait J, Fernández L, Fernández JC, Alemán C, Effects of policosanol in patients with type II hypercholesterolemia and additional coronary risk factors, Clin Pharmacol Ther, 65, 1999, 439-447.

42. Prat H, Roman O, Pino E, Comparative effects of policosanol and two HMG-CoA reductase inhibitors on type II hypercholesterolemia, Rev Med Chil, 127, 1999, 286-494.

43. Nikitin IP, Slepchenko NV, Gratsianskii NA, Nechaev AS, Syrkin AL, Poltavskaia MG, Results of the multicenter controlled study of the hypolipidemic policosanol in Russia, Ter Arkh, 72, 2000, 7–10.

44. Wang Y, Kuanman KE, Wang Hia L, Jiao Y, Zhao X, Sun N, Efficacy and safety of policosanol and pravastatin in treatment of hyperlipidemia in Chinese patients, J New Drugs Clin Res, 2, 2008, 124-129.

45. Liu S, Tan MY, Zhao SP, Rong H, Effects of policosanol on serum lipids and heme oxygenase-1 in patients with hyperlipidemia, Zhonghua Xin Xue Guan Bing Za Zhi, 40, 2012, 840-843.

46. Tang M, Wu SZ, Gong X, Effects of policosanol combined with simvastatin on serum lipids and sex hormones in male patients with hyperlipidemia, Zhonghua Xin Xue Guan Bing Za Zhi, 4, 2013, 488-492.

Source of Support: Nil, **Conflict of Interest:** None.