Randomized Comparative Study of the Effects of Treatment with Once-daily, Niacin Extended-release/Lovastatin and with Simvastatin on Lipid Profile and Fibrinolytic Parameters in Taiwan

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Hyperlipidemia can be effectively treated either with niacin or HMG-CoA reductase inhibitor (statin), or a combination of both. Few reports showed the effects of the combination regimen with niacin and statin on hemostatic functions. We conducted a single-center, double-blind, double-dummy, randomized, two-arm study to assess the effects of the niacin extended-release/lovastatin therapy in a fixed-dose formulation and of simvastatin on lipid lowering and two fibrinolytic parameters, fibrinogen and d-dimer. All patients were enrolled according to NCEP-ATP III guidelines and underwent a placebo run-in period of 4 weeks before being randomized to either niacin extended-release/lovastatin tablets (500/20 mg) once daily ($n = 36$) or simvastatin capsule (20 mg) once daily ($n = 34$). After 16 weeks of treatment, both groups of patients showed significantly reduced low-density lipoprotein cholesterol and total cholesterol (LDL-C, $p < 0.001$ and < 0.001, respectively, $p = 0.159$ between the groups; TC, $p < 0.001$ and < 0.001, respectively, $p = 0.018$ between the groups). Both drugs were well tolerated. Only in the group treated with niacin extended-release/lovastatin was fibrinogen concentration significantly reduced after treatment (2.48 ± 0.65 to 1.99 ± 0.62 g/L, $p = 0.008$). No difference was found with d-dimer in either group. This study shows that both niacin extended-release/lovastatin and simvastatin are effective and well-tolerated lipid-lowering drugs in Taiwanese patients with dyslipidemia. A combinational treatment with niacin extended-release/lovastatin may provide additional benefit in fibrinolysis.

Key Words: niacin, statin, fibrinolysis, dyslipidemia, fibrinogen
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Hyperlipidemia represents a determinant in the development of atherosclerosis and an important risk factor for cardiovascular disease. There is a curvilinear relationship between total serum cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and deaths from coronary heart disease (CHD) [1]. Increasing levels of high-density lipoprotein cholesterol (HDL-C) are associated with a reduced relative risk of CHD. Therefore, the LDL/HDL cholesterol ratio is useful in assessing the absolute risk of CHD.

Many large trials showed that lipid lowering can reduce CHD morbidity and mortality [2,3]. HMG-CoA reductase inhibitor (statin) can effectively reduce TC, LDL-C, triglycerides (TG), and increase HDL-C. Pharmacologic treatment with statin drugs was shown to greatly improve cardiovascular morbidity and mortality in primary and secondary prevention studies [4]. Niacin is recognized as

the most potent agent available to increase HDL-C. It also decreased LDL-C and total mortality in secondary prevention trials [5].

Numerous studies have demonstrated that disturbances of coagulation and fibrinolysis contribute to the development and progression of atherosclerosis. It has been established that the benefits of statin therapy in cardiovascular disease can be explained not only by the lipid-lowering potential, but also by nonlipid-related mechanisms and is known as statin pleiotropic effects, which are partly achieved by their fibrinolytic ability [6]. Niacin, when added to statins, can reduce TG, increase HDL-C, and reduce non-HDL-C to a greater extent than statin monotherapy [7]. We had previously reported that statin could modulate fibrinolysis [8]. However, the influence of a combination regimen of statin and niacin on hemostatic parameters is unclear.

Combined use of niacin with a statin is an attractive option, since these types of medication have the best records in clinical trials for reduction in cardiovascular events and improvement in progression/regression of coronary lesions [7]. Few studies have investigated the effect of combination treatment on lipid profile in Orientals. This study investigates the lipid-lowering efficacy and safety of niacin extended-release plus lovastatin therapy in a fixed-dose formulation and simvastatin administered orally once daily for 16 weeks to dyslipidemia patients in Taiwan. We also tested the change of the two fibrinolytic parameters—fibrinogen and *d*-dimer.

Subjects and Methods

This was a single-center, double-blind, double-dummy, randomized, two-arm study comparing the efficacy and safety of niacin extended-release/lovastatin tablets (500/20 mg) and simvastatin capsule (20 mg) for the treatment of dyslipidemia. Physical examination was performed every 4 weeks during the visit. Blood biochemistry and lipid profile were measured at the central laboratory in Kaohsiung Medical University Chung-Ho Memorial Hospital. During each visit, general open-ended questions were given to monitor any occurrences of adverse events. The study was approved by the institutional review committee of Kaohsiung Medical University Hospital. Each study participant signed an informed consent form.

The inclusion criteria were: (1) ≥ 20 years of age; (2) failure to control LDL-C level under the 4-week therapeutic lifestyle changes (TLC); (3) hyperlipidemia diagnosed according to National Cholesterol Education Program

Adult Treatment Panel III (NCEP-ATP III) guidelines: CHD and CHD risk equivalents (i.e. 10-year risk > 20%) with LDL-C ≥ 130 mg/dL, ≥ 2 risk factors and 10-year risk 10–20% with LDL-C ≥ 130 mg/dL, ≥ 2 risk factors and 10-year risk < 10% with LDL-C ≥ 160 mg/dL, ≤ 1 risk factor with LDL-C ≥ 190 mg/dL [9]; (4) receiving concomitant treatment other than lipid-control treatment that was known to affect lipid level and dose maintained unchanged throughout the study; (5) male/female subject with reproductive potential is under appropriate contraception; (6) compliance and geographic proximity to the study site allowing adequate follow-up; (7) willing to participate in the trial and sign a written consent.

Those who met the above criteria were excluded if any of the following was observed: (1) TG > 500 mg/dL; (2) breast feeding in female subject; (3) pregnancy or not exercising appropriate birth control during course of study; (4) type I diabetes; (5) uncontrolled type II diabetes requiring insulin treatment; (6) uncontrolled hypertension (systolic blood pressure > 180 mmHg or diastolic blood pressure > 110 mmHg); (7) uncontrolled hypothyroidism; (8) diagnosis of acute myocardial infarction within the proceeding 3 months; (9) insufficient renal function (serum creatinine > 2.0 mg/dL); (10) insufficient liver function (aspartate aminotransferase, AST/alanine aminotransferase, ALT > 2 times normal); (11) diagnosis of severe peptic ulcer disease; (12) gout attack and hyperuricemia within 1 month preceding randomization; (13) not able to stop concomitant lipid-control treatment during the study; (14) history of hypersensitivity to product being investigated; and (15) drug or alcohol abuse.

The whole duration of this trial was 25 weeks (i.e. 5-week wash out, 16-week drug treatment, and 4-week follow-up period). During the 5-week wash out (placebo run-in) period, each subject discontinued their lipid-lowering medicine and engaged TLC. Patients were randomized to one of the following parallel treatment groups: niacin extended-release plus lovastatin tablets (500/20 mg) or simvastatin capsule (20 mg). The initial 4 weeks was a titration period. The dose was adjusted according to the treatment goal suggested by the NCEP-ATP III guidelines, i.e. CHD and CHD risk equivalents (i.e. 10-year risk > 20%) to LDL-C < 100 mg/dL, ≥ 2 risk factors to LDL-C < 130 mg/dL, ≤ 1 risk factor to LDL-C < 160 mg/dL [9]. Patients who did not meet the above criteria after the 4-week treatment were advanced to the double strength regimen (niacin extended-release plus lovastatin tablets 1,000/40 mg or simvastatin capsule 40 mg).

Laboratory evaluation was done at screening, every 4-week visit after active medication, and the end of study. Fasting blood samples (8-hour fast) were collected for lipid profile and biochemistry analysis. Whole blood (10 mL) was collected in sodium citrate tubes and centrifuged for fibrinolytic parameters. Plasma was frozen at –80°C until use. Fibrinolytic parameter analysis was done at the end of the study. Fibrinogen was measured according to the Clauss clotting method, and *d*-dimer concentration was measured by the immunoturbidmetric method (Diagnostica Stago, France).

The primary endpoint of this study was efficacy of LDL-C decreasing after 16 weeks with either niacin extended-release plus lovastatin or simvastatin treatment. The secondary endpoints were the TC, TG, and HDL-C changes, safety profile and alteration of fibrinolytic parameters (fibrinogen and *d*-dimer).

Statistical analysis

All data were expressed as mean ± standard deviation (SD). All tests were two-sided. A $p < 0.05$ was considered statistically significant. Chi-square test and Wilcoxon's rank-sum test were used to compare categorical data and nonparametric data, respectively. The *t* test was used to analyze continuous variables. The primary analysis for efficacy endpoints was performed based on the intent-to-treat (ITT) population. For primary and secondary endpoints, percent changes from baseline were compared between treatment groups by using ANCOVA with one fixed factor for treatment group and the responding baseline value as the covariate. SPSS version 11.0 (SPSS Inc, Chicago, IL, USA) for Windows was used for statistical analysis.

RESULTS

Baseline data

Overall, 164 subjects were screened for enrollment into this study. Seventy met the inclusion criteria and were randomized into the two scheduled treatment groups: 36 subjects in the niacin extended-release plus lovastatin group *vs*. 34 subjects in the simvastatin group. During the study, two subjects did not take any study medicine (1 subject in niacin extended-release plus lovastatin group; 1 subject in simvastatin group). Seven subjects had no post-treatment evaluation (4 subjects in combination group; 3 subjects in simvastatin group). Finally, the ITT group in this study included 61 subjects (31 subjects in combination group *vs*. 30 subjects in simvastatin group). The baseline characteristics of these 61 participants are given in Table 1. There was no difference between patients taking niacin extended-release plus lovastatin and simvastatin regarding sex, age, body weight, height, systolic/diastolic blood pressure, duration of hyperlipidemia, and criteria for enrollment.

During the study, 16 subjects withdrew from the study (11 subjects in combination group *vs*. 5 subjects in simvastatin group). Fourteen subjects withdrew their consent (10 subjects in combination group and 4 subjects in simvastatin group) for nonadverse event-related personal reasons or were lost to follow-up. One subject from the combination group was withdrawn from the study because of ineffective test drug (LDL-C level: 200 mg/day after doubling dose). A subject in the simvastatin group discontinued treatment due to skin itching. The study was completed, including 25 subjects from the combination group and 29 subjects from the simvastatin group.

Table 1. Baseline characteristics*			
	Lovastatin plus niacin (*n* = 31)	Simvastatin (*n* = 30)	*p*
Sex (male, %)	48	60	0.444
Age (yr)	58.2 ± 9.1	58.5 ± 9.7	0.898
Height (cm)	159.6 ± 7.7	161.9 ± 7.5	0.237
Weight (kg)	64.6 ± 12.9	65.0 ± 10.4	0.881
Systolic BP	134.6 ± 18.7	135.7 ± 13.1	0.739
Diastolic BP	81.7 ± 10.5	83.1 ± 9.0	0.942
Duration of hyperlipidemia (mo)	18 ± 3.0	18.9 ± 2.5	0.919
Enrollment criteria (%)			
CHD and CHD risk equivalents	71	63	
2+ risk factors and 10-year risk 10–20%	26	33	
2+ risk factors and 10-year risk < 10%	3	0	0.578
0–1 risk factor	0	3	

*Values are shown as mean ± standard deviation. BP = blood pressure; CHD = coronary heart disease.

Table 2. Lipid profile before and after treatment*

	Baseline	12th week	*p*
LDL-C			
Niacin ER plus lovastatin	161.4 ± 21.6	110.8 ± 25.2	< 0.001
Simvastatin	159.9 ± 25.6	102.1 ± 26.0	< 0.001
TC			
Niacin ER plus lovastatin	241.8 ± 26.2	191.0 ± 32.1	< 0.001
Simvastatin	238.8 ± 28.3	172.7 ± 28.7	< 0.001
HDL-C			
Niacin ER plus lovastatin	45.2 ± 11.7	49.2 ± 12.5	0.003
Simvastatin	42.7 ± 8.6	43.7 ± 10.7	0.371
TG			
Niacin ER plus lovastatin	129.9 ± 68.8	118.4 ± 47.2	0.672
Simvastatin	155.7 ± 83.2	115.2 ± 52.3	0.017

*Values are shown as mean ± standard deviation. LDL-C = low-density lipoprotein cholesterol; ER = extended-release; TC = total cholesterol; HDL-C = high-density lipoprotein cholesterol; TG = triglyceride.

Lipid profile

Both treatments significantly reduced LDL-C and TC compared with baseline (Table 2). LDL-C decreased in patients taking niacin extended-release plus lovastatin from 161.4 ± 21.6 to 110.8 ± 25.2 mg/dL ($p < 0.001$). TC dropped from 241.8 ± 26.2 to 191.0 ± 32.1 mg/dL ($p < 0.001$). In the simvastatin group, LDL-C decreased from 159.9 ± 25.6 to 102.1 ± 26.0 mg/dL ($p < 0.001$), and TC from 238.8 ± 28.3 to 172.7 ± 28.7 mg/dL ($p < 0.001$). Treatment with niacin extended-release plus lovastatin, but not with simvastatin, significantly increased HDL-C compared with baseline (45.2 ± 11.7 to 49.2 ± 12.5 mg/dL, $p = 0.003$ and 42.7 ± 8.6 to 43.7 ± 10.7, $p = 0.371$, respectively). Treatment with simvastatin, but not with niacin extended-release plus lovastatin, significantly reduced TG compared with baseline (155.7 ± 83.2 to 115.2 ± 52.3 mg/dL, $p = 0.017$ and 129.9 ± 68.8 to 118.4 ± 47.2, $p = 0.672$, respectively).

There was no difference in LDL-C and TG change between the combination treatment and simvastatin (−30.5 ± 17.7 *vs*. −36.0 ± 13.7% for LDL-C, $p = 0.159$ and 3.2 ± 42.1 *vs*. −17.1 ± 36.8% for TG, $p = 0.136$). There was a significant difference in TC and HDL change between the groups (−20.6 ± 13.7 *vs*. −27.5 ± 9.5% for TC, $p = 0.018$, and 10.4 ± 18.0 *vs*. 2.2 ± 13.4%, $p = 0.029$ for HDL).

Tolerability and safety

The severity of adverse events based on the body systems was dependent on patients' description and classified as mild, moderate, and severe. The adverse events were mostly mild in severity and are shown in Table 3. No statistically significant difference was found between the two groups. No drug-related adverse event was reported in this study. The study medications in the two treatment groups were generally well tolerated.

There were no significant changes in the biochemistry data that include BUN, creatinine, and total bilirubin. AST and ALT increased in subjects receiving combination treatment but not in those taking simvastatin (26.26 ± 10.24 to 32.50 ± 13.30 U/L, $p = 0.005$ and 26.55 ± 11.48 to 33.65 ± 16.05 U/L, $p = 0.023$, respectively). However, the mean values of each parameter were within the normal range. No subject was required to discontinue treatment at the investigator's discretion.

Fibrinolytic parameters

Of the 54 patients who completed the trial, five in the lovastatin plus niacin group and seven in the simvastatin group had no adequate blood sample for examination of fibrinolytic parameters. The remaining 42 patients (20 in niacin extended-release plus lovastatin; 22 in simvastatin group) received evaluation of fibrinolytic parameters. Fibrinogen significantly decreased with the combination treatment (2.48 ± 0.65 to 1.99 ± 0.62 g/L, $p = 0.008$), but not with simvastatin (2.71 ± 0.72 to 2.68 ± 0.75 g/L, $p = 0.846$) (Figure 1). There was no change in *d*-dimer after both treatments (0.30 ± 0.12 to 0.35 ± 0.19 μg/mL, $p = 0.055$ in combination group; 0.33 ± 0.17 to 0.29 ± 0.14 μg/mL, $p = 0.155$ in simvastatin group) (Figure 2).

Table 3. Adverse events

	p	Niacin extended-release plus lovastatin				Simvastatin			
		Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Cardiovascular system									
Arrhythmia	0.75	3 (8.6%)	0 (0.0%)	0 (0.0%)	3 (8.6%)	1 (3.0%)	0 (0.0%)	0 (0.0%)	1 (3.0%)
Arteriosclerosis	0.59	4 (11.4%)	0 (0.0%)	0 (0.0%)	4 (11.4%)	2 (6.1%)	0 (0.0%)	0 (0.0%)	2 (6.1%)
Cardiovascular disorder	0.13	8 (22.9%)	1 (2.9%)	0 (0.0%)	9 (25.7%)	11 (33.3%)	1 (3.0%)	0 (0.0%)	12 (36.4%)
Myocardial ischemia	0.65	3 (8.6%)	0 (0.0%)	0 (0.0%)	3 (8.6%)	2 (6.1%)	0 (0.0%)	0 (0.0%)	2 (6.1%)
Palpitation	0.49	6 (17.1%)	0 (0.0%)	0 (0.0%)	6 (17.1%)	2 (6.1%)	0 (0.0%)	0 (0.0%)	2 (6.1%)
Pericardial effusion	0.75	1 (2.9%)	0 (0.0%)	0 (0.0%)	1 (2.9%)	3 (9.1%)	0 (0.0%)	0 (0.0%)	3 (9.1%)
Vascular disorder	0.67	5 (14.3%)	0 (0.0%)	0 (0.0%)	5 (14.3%)	1 (3.0%)	0 (0.0%)	0 (0.0%)	1 (3.0%)
Digestive system									
Dyspepsia	0.54	2 (5.7%)	0 (0.0%)	0 (0.0%)	2 (5.7%)	5 (15.2%)	0 (0.0%)	0 (0.0%)	5 (15.2%)
Flatulence	0.65	2 (5.7%)	0 (0.0%)	0 (0.0%)	2 (5.7%)	3 (9.1%)	0 (0.0%)	0 (0.0%)	3 (9.1%)
Nausea	0.75	1 (2.9%)	0 (0.0%)	0 (0.0%)	1 (2.9%)	3 (9.1%)	0 (0.0%)	0 (0.0%)	3 (9.1%)
Musculoskeletal system									
Edema/cramp/pain	0.71	7 (20.0%)	0 (0.0%)	1 (2.9%)	8 (22.9%)	2 (6.1%)	0 (0.0%)	0 (0.0%)	2 (6.1%)
Nervous system									
Dizziness	0.07	8 (22.9%)	0 (0.0%)	0 (0.0%)	8 (22.9%)	7 (21.2%)	4 (12.1%)	0 (0.0%)	11 (33.3%)
Insomnia	0.59	4 (11.4%)	0 (0.0%)	0 (0.0%)	4 (11.4%)	2 (6.1%)	0 (0.0%)	0 (0.0%)	2 (6.1%)
Respiratory system									
Cough and sputum	0.30	3 (8.6%)	0 (0.0%)	0 (0.0%)	3 (8.6%)	8 (24.2%)	0 (0.0%)	0 (0.0%)	8 (24.2%)
Pharyngitis	0.50	3 (8.6%)	0 (0.0%)	0 (0.0%)	3 (8.6%)	4 (12.1%)	0 (0.0%)	0 (0.0%)	4 (12.1%)
Skin and appendages									
Pruritus or rash	0.59	2 (5.7%)	0 (0.0%)	0 (0.0%)	2 (5.7%)	4 (12.1%)	0 (0.0%)	0 (0.0%)	4 (12.1%)

DISCUSSION

This study had three findings. First, both niacin extended-release plus lovastatin and simvastatin were shown to be comparatively effective in decreasing LDL-C and TC. Second, both treatments were well tolerated in our study subjects. Third, treatment with niacin extended-release plus lovastatin may provide additional benefits in fibrinolysis.

Research into experimental animals, laboratory investigations, epidemiology, and genetic forms of hypercholesterolemia indicate that elevated LDL-C is a major cause of CHD [1]. In addition, recent clinical trials robustly show that LDL-lowering therapy reduces the risk for CHD [2,3] and, hence, the NCEP-ATP III continues to identify elevated LDL-C as the primary target of cholesterol-lowering therapy. As a result, the primary goals of therapy and the cut-off points for initiating treatment are stated in terms of LDL [9]. Lessons from recent endpoint trials of lipid-lowering drugs indicated that patients at very high

risk for CHD benefit from treatment that decreases LDL-C plasma levels to ≤ 70 mg/dL, that patients with ≥ 2 risk factors benefit from treatment that decrease plasma LDL-C to < 100 mg/dL, and that a significant reduction in CHD event rates is most often associated with a minimum plasma LDL-C reduction of 30%. Recently, the NCEP-ATP III recommendations were amended to incorporate these lessons [10]. To reach these more aggressive goals and plasma LDL-C reductions, more aggressive therapies and even combination therapy will be required.

Both statin and niacin have demonstrated clinical trial evidence of reducing coronary artery disease events and overall mortality [2–5]. Because statins and niacin may have potentially complementary actions, the combination of these two lipid-lowering drugs with different mechanisms of action has been studied, demonstrating greater reductions in LDL-C than with each agent alone [11–14]. Nicotinic acid is known as the most effective lipid drug for raising values of plasma HDL-C [9]. In an informative angiographic clinical
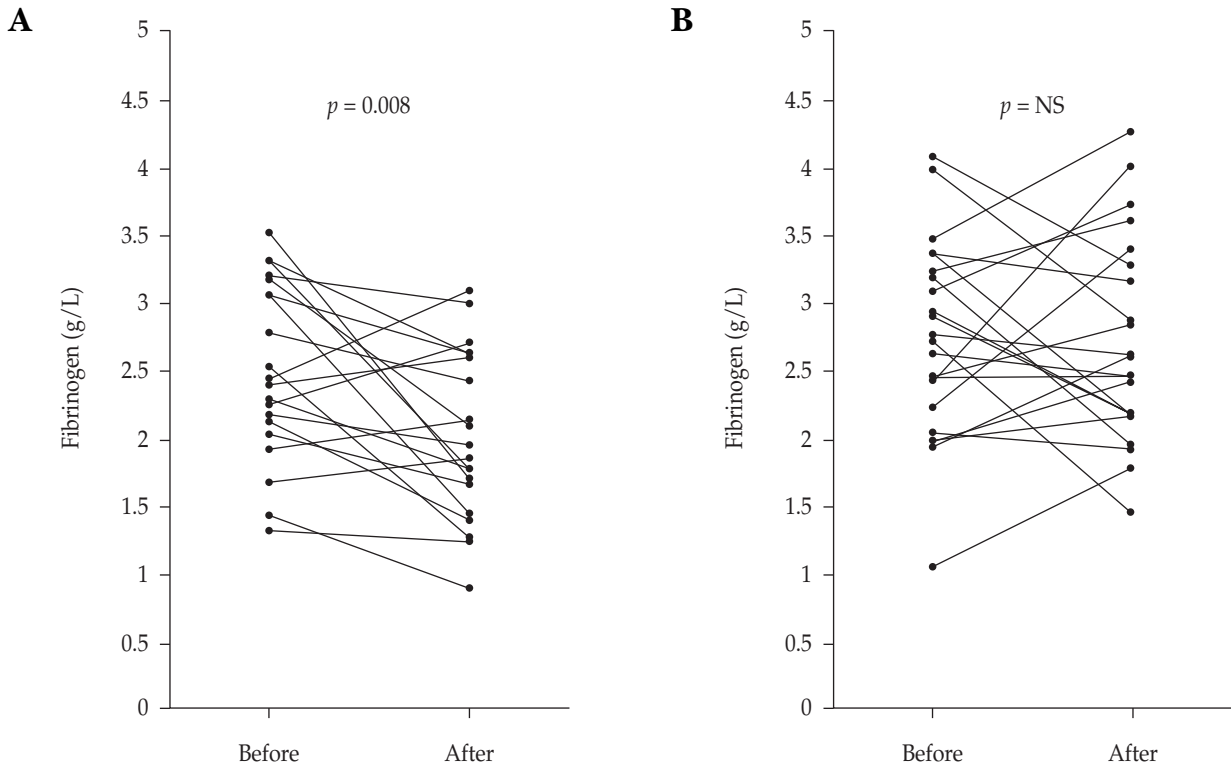
A

B

Figure 1. Fibrinogen change before and after treatment: (A) niacin extended-release plus lovastatin; (B) simvastatin.
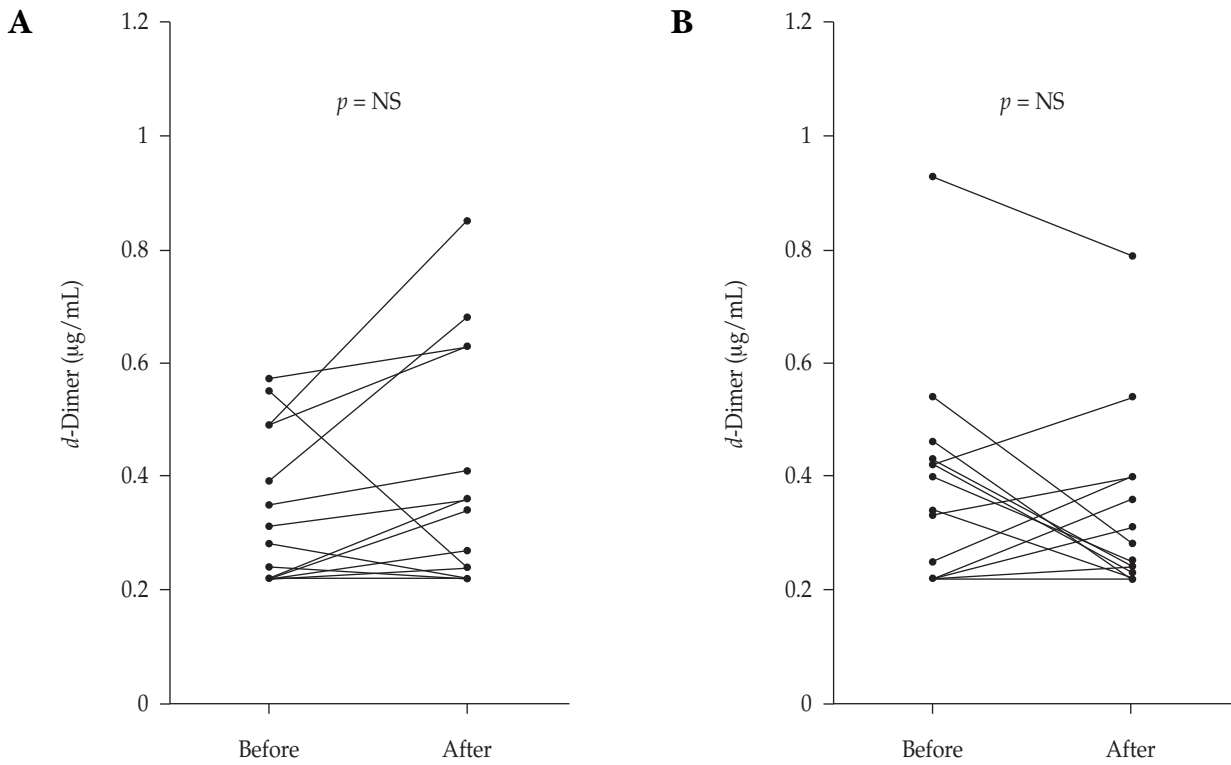
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Figure 2. d-*Dimer change before and after treatment: (A) niacin extended-release plus lovastatin; (B) simvastatin.*

trial in men and women with low values of plasma HDL-C cholesterol, combination treatment with nicotinic acid and statin was more effective in significantly increasing HDL-C, decreasing LDL-C and coronary angiographic progression compared with placebo [15]. Previous study showed that a once-daily niacin extended-release/lovastatin fixed-dose combination was effective in reducing LDL-C and increasing HDL-C in a Caucasian population [16]. In this study, the same combination treatment was also effective in decreasing LDL-C and increasing HDL-C in a Taiwanese population.

This combination therapy, however, may be associated with serious side effects as concomitant use of niacin and statin is associated with an increased risk of myopathy. Additionally, niacin used either in monotherapy or co-administration therapy is associated with vasodilatory side effects that are intolerable to some patients [17]. This face flush has been shown to lead to discontinuation of therapy in patients taking niacin [16,18]. In our study population, no subjects complained of significant face flush. There have been several reports indicating a higher incidence of liver toxicity with sustained release of nicotinic acid [19]. Although the mechanism of hepatic injury remains unknown, evidence implicates a dose-related toxicity and not a hypersensitivity reaction [20]. The hepatotoxic effects of niacin are usually transient with evidence of both cholestasis and hepatocellular injury, and histopathologic findings are consistent with centrilobular cholestasis and parenchymal necrosis [21]. Although there were mild elevations of liver enzymes, no subject in this study was required to discontinue treatment at the investigator's discretion. Few reports have discussed the tolerability of combination treatment with niacin and statin in Orientals. Our study showed that combination therapy was well tolerated, but with mild liver function impairment, in the Taiwanese population.

There was some basic clinical evidence that reductions in cardiovascular risk with statin are dependent on mechanisms beyond cholesterol reduction alone, such as modulation of procoagulant activity [22]. Recent evidence suggests that most of these effects are mediated by the inhibitory effect of statins on isoprenoid synthesis [23]. Limited studies have investigated the niacin effect on fibrinolytic activity. Some results suggest that niacin may potentiate fibrinolysis [24,25]. The mechanism of this favorable effect in fibrinolysis after niacin treatment is still unclear. In our study, those who received combination treatment had significantly decreased fibrinogen after 16 weeks' treatment, although niacin extended-release plus lovastatin and simvastatin had the same degree of LDL-C

and TC lowering. However, the result is preliminary and more work will be necessary to clarify the effects of niacin and combination treatment on fibrinolytic function.

The major limitation of our investigation is the small number of patients. Treatment with niacin extended-release plus lovastatin may improve the fibrinolytic profile in patients with dyslipidemia, but this requires confirmation from more extensive clinical data.

CONCLUSION

Once-daily administration of niacin extended-release plus lovastatin is effective and is a well-tolerated lipid-lowering agent in Taiwanese patients with dyslipidemia. Sixteen-week treatment with niacin extended-release plus lovastatin also significantly reduced fibrinogen. This effect may provide additional cardiovascular benefit.

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比較 Niacin Extended-release/Lovastatin 與 Simvastatin 對降血脂及血栓溶解因子的影響

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Niacin，HMG-CoA reductase inhibitor (statin) 及二者合併使用可有效的控制血脂。少有研究探討二者合併對血栓溶解因子的影響。我們進行一單中心，雙盲的研究來探討 niacin extended-release/lovastatin 及 simvastatin 對血脂及血栓溶解因子 (纖維原與 d 雙體) 的影響。所有的病人根據 NCEP-ATP III 的準則接受 4 週安慰劑後隨機分給每天 niacin extended-release/lovastatin (500/20 mg) 或 simvastatin (20 mg) 的治療。16 周後兩群病人皆顯著下降低密度膽固醇 (LDL-C) 及總膽固醇 (TC) (LDL-C，$p < 0.001$ & $p < 0.001$；兩群間 $p = 0.092$；TC，$p < 0.001$ & $p < 0.001$，兩群間 $p = 0.504$)。兩種治療都有良好的耐受性。只有在接受 niacin extended-release/lovastatin 治療的病人，纖維原濃度明顯下降 (2.48 ± 0.65 to 1.99 ± 0.62 g/L，$p = 0.008$)。d 雙體在兩群病人都無顯著變化。本研究顯示 niacin extended-release/lovastatin 與 simvastatin 治療台灣高血脂病人是有效且有好的耐受性。合併治療可能提供額外血栓溶解的好處。