Efficacy of simvastatin compared with atorvastatin in patients with hyperlipidaemia in Kurdistan

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Abstract

Background and objectives: Lowering the blood cholesterol and low density lipoprotein levels may reduce the risk of coronary heart disease. This study was designed to evaluate the effect of lipid-lowering therapy by simvastatin 20 mg versus atorvastatin 20mg on patients suffering from hyperlipidemia.

Method: This study is 16-weeks duration included 75 patients with hyperlipidemia. Patients were assigned randomly to receive either simvastatin 20 mg/day group (1), or atorvastatin 20 mg/day group (2). After 12 hours fasting, lipid profile, atherogenic index and alanine aminotransferase were assessed for the patients at baseline, 8-weeks and at the end of 16 -weeks of treatment.

Results: After therapy for both groups of patients, as compared to the levels at the baseline, the serum total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-C) and very low density lipoprotein cholesterol (VLDL-C) were significantly reduced while high density lipoprotein cholesterol (HDL-C) was significantly increased. Serum alanine aminotransferase (ALT) increased by both groups of treatment with no significant differences between the two modes of treatment.

Conclusion: After treatment with simvastatin 20 mg and atorvastatin 20 mg, there were a reduction in total cholesterol, triglyceride, LDL-C, and VLDL-C, and an increase in HDL-C in both groups. Comparing the two types of treatment, atorvastatin 20 mg was more effective in lowering triglyceride and VLDL-C than simvastatin 20 mg while Simvastatin led to greater reduction in LDL-C. Both modes of treatment were well tolerated by the patients.

Keywords: hyperlipidaemia, atherogenic index, atorvastatin, simvastatin, alanine aminotransferase.

Introduction

There is a wealth of evidence suggesting that lowering low density lipoprotein cholesterol LDL-C reduces the risk of cardiovascular disease CVD. [1-4] Both European and US guidelines for CVD prevention recommend the use of 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins) as a first-line therapy for dyslipideamia.[5,6] Despite the proven benefits of LDL-C reduction, lipid management is suboptimal and many patients fail to achieve recommended LDL-C goals. The most effective statin at the lowest dose would represent a simple, effective treatment strategy, enabling more patients to achieve goals without the need for dose titration.[7,8] The aim of the study was to compare simvastatin 20mg/day and atorvastatin 20mg/day for their total cholesterol and LDL-C- lowering efficacy in hyperlipidemic patients. The doses chosen for the study were generally recommended the start doses of simvastatin and atorvastatin. [9]

Method

This study is the first trial in Iraqi region of Kurdistan to compare the lipid-lowering efficacy of two marketed HMG-CoA reductase inhibitors. It was a 16-weeks comparative study evaluating the efficacy

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of once-daily dose of simvastatin 20 mg compared with once-daily dose of atorvastatin 20 mg. The study conducted at Rizgary Teaching Hospital in Erbil city and covered 75 untreated hyperlipidemic male and female patients 31 to 65 years old. Patients were assigned randomly to receive either simvastatin 20mg/day this group comprised of 45 patients, the second group was 30 patients receiving atorvastatin 20mg/day. Any Patient with other diseases or on other medications that might affect the study was excluded. Fifty five (55) male and female normal subjects (normolipidemic) were included as a control group. Their ages ranged between 25-43 years and divided into 25 as control with simvastatin therapy and 30 with atorvastatin. Fasting blood samples of both groups of patients (before treatment and after) were collected. Serum was separated by centrifugation at 3000 rpm for 5 minutes then total cholesterol, triglycerides, LDL-C, VLDL-C, HDL-C, and ALT were estimated by enzymatic colorimetric method.

Results

In Table (1) the effect of simvastatin 20 mg on lipid profile, serum ALT, and atherogenic index for group (1) are shown before, after 8 weeks and 16 weeks of treatment. A significant reduction was observed for total serum cholesterol, triglycerides, LDL-C, VLDL-C and atherogenic index TC/HDL and a significant increase was observed for HDL-C by performing a comparison between baseline, after 8 weeks and 16-weeks of treatment with simvastatin. Serum ALT had increased insignificantly after 8 weeks of treatment, but had significantly increased after 16 weeks of treatment yet within normal ranges.

Table 1: Effects of Simvastatin 20 mg on serum total cholesterol, triglycerides, high density lipoproteins, low density lipoproteins, very low density lipoproteins, alanine aminotransferase, and atherogenic index (TC/HDL) before, after 8 and 16- weeks of treatment.

Parameters	Control (n=25)	Group (1) patients treated with simvastatin (n=45)		
		Before treatment	After 8 weeks of Treatment	After 16 weeks of Treatment
TC mmol/L	4.03±0.76[a]	6.19±0.98[b]	5.13±0.65[c]	4.13±0.46[d]
TG mmol/L	1.79±0.22[a]	2.80±0.50[b]	2.51±0.42[c]	2.23±0.46[d]
HDL-C mmol/L	1.24±0.15[a]	0.89±0.14[b]	0.98±0.13[c]	1.10±0.11[d]
LDL-C mmol/L	2.42±0.8[a]	3.96±0.88[b]	3.01±0.61[c]	2.19±0.41[d]
VLDL-C mmol/L	0.36±0.04[a]	0.59±0.01[b]	0.50±0.08[c]	0.44±0.07[d]
Atherogenic index TC/HDL	3.32±0.82[a]	7.07±1.4[b]	5.30±0.93[c]	3.95±0.50[d]
ALT IU/L	10.16±1.86[a]	15.33±4.11[b]	15.73±2.77[a]	22.77±4.64[a]

***Data represented by mean ± SD.**
***Values with non-identical superscript (a, b, c, d) are representing significant difference at level P< 0.05.**

Table (2) shows the effect of atorvastatin 20 mg on serum, total cholesterol, triglycerides, LDL-C, VLDL-C, HDL-C, ALT, and atherogenic index for group (2) after 8 and 16 weeks of treatment with atorvastatin as compared before starting the treatment .It was observed that atherogenic index, serum lipid profile, (except HDL-C) were significantly reduced while serum HDL-C was significantly increased after 8 and16weeks of treatment- in comparison to before treatment (baseline); and at the same time a significant difference was also observed in comparison to control group. ALT has significantly changed after 8 weeks and 16 weeks of treatment when compared before starting the treatment, while no significant difference when compared to control group**.**

In Table (3) the percent changes of serum lipid profile were compared from the baseline to the 16th weeks between the two groups showed that after 8 weeks of treatment, atorvastatin produced numerically greater reduction in the mean percent of total cholesterol and LDL-C but with statistically significant differences in the mean percent of triglyceride, VLDL-C and HDL-C. After 16 weeks there were no differences in comparing the mean percent between the two modes of treatment for total cholesterol, and HDL-C, but with statistically significant differences for atorvastatin than simvastatin in triglyceride and VLDL-C, while simvastatin shows statistically significant result in the percent reduction in LDL-C compared to atorvastatin.

Table 2: Effects of Atorvastatin 20 mg on serum total cholesterol, triglycerides, high density lipoproteins, low density lipoproteins, very low density lipoproteins, alanine aminotransferase, and atherogenic index (TC/HDL) before, after 8 and 16- weeks of treatment.

Parameters	**Control (n=30)**	**Group (2) patients treated with Atorvastatin (n=30)**		
		Before treatment	**After 8 weeks of Treatment**	**After 16 weeks of Treatment**
TC mmol/L	3.71±0.20^{a}	6.41±0.91^{b}	5.18±0.53^{c}	4.47±0.39^{d}
TG mmol/L	1.54±0.17^{a}	2.90±0.44^{b}	2.30±0.34^{c}	1.99±0.33^{d}
HDL-C mmol/L	1.21±0.09^{a}	0.97±0.12^{b}	1.07±0.12^{c}	1.14±0.12^{d}
LDL-C mmol/L	1.74±0.25^{a}	4.10±0.98^{b}	3.05±0.57^{c}	2.41±0.40^{d}
VLDL-C mmol/L	0.30±0.03^{a}	0.57±0.08^{b}	0.46±0.06^{c}	0.39±0.06^{d}
Atherogenic Index TC/HDL	2.97±0.29^{a}	6.66±1.15^{b}	4.88±0.72^{c}	3.91±0.58^{d}
ALT IU/L	15.1±3.12^{a}	12.86±3.29^{b}	14±3.02^{a}	15.4±3.15^{a}

***Data represented by mean ± SD.**

***Values with non-identical superscript (a, b, c, d) are representing significant difference at level P< 0.05.**

Table 3: Change in lipid variables from the baseline by comparing the efficacy of simvastatin 20 mg versus atorvastatin 20mg.

Drug			Simvastatin (20 mg)	Atorvastatin (20 mg)
Reduction in Total cholesterol	After 8 weeks of Treatment	Percent mmol / L	17.12 (5.134 ± 0.096)	19.18 (5.183± 0.097)
	After 16 weeks of Treatment	Percent mmol / L	33.28 (4.31 ± 0.068)	30.26 (4.47 ± 0.07)
Reduction in Triglyceride	After 8 weeks of Treatment	Percent mmol / L	10.36 (2.507 ± 0.063)	20.69 (2.30 ± 0.062)*
	After 16 weeks of Treatment	Percent mmol / L	20.35 (2.22 ± 0.500)	31.38 (1.99 ± 0.06)*
Reduction in LDL-C	After 8 weeks of Treatment	Percent mmol / L	23.99 (3.006 ± 0.914)	25.61 (3.051 ± 0.01)
	After 16 weeks of Treatment	Percent mmol / L	44.7 (2.186± 0.06)*	41.22 (2.414± 0.07)
Reduction in VLDL-C	After 8 weeks of Treatment	Percent mmol / L	15.25 (0.50 ± 0.013)	19.30 (0.46± 0.0123)*
	After 16 weeks of Treatment	Percent mmol / L	25.4 (0.44 ± 0.01)	31.58 (0.39 ± 0.012)***
Increase in HDL-C	After 8 weeks of Treatment	Percent mmol / L	10.11 (0.98 ± 0.19)	10.31 (1.074 ± 0.23)*
	After 16 weeks of Treatment	Percent mmol / L	23.6 (1.097 ± 0.02)	17.52 (1.143 ± 0.022)

Data representing by mean ±SD.
*** Representing significant difference at level p < 0.05.**
***** Representing highly significant difference at level P < 0.001.**

Discussion

It was well established that cholesterol plays a major role in a person's heart health. Elevation of circulating levels of triglyceride-rich VLDL and cholesterol-rich LDL is a major risk factor for coronary heart disease and stroke. The major effect of statins is in reducing LDL-C concentrations, primarily mediated by inhibition of the rate -limiting step in cholesterol biosynthesis resulting in an increase in LDL receptors in the liver[10], also can reduce triglycerides and increase HDL-C. [11] The Table (1) shows that the serum, total cholesterol, and LDL-C were significantly reduced in hyperlipidemic patients treated with simvastatin after 8 and 16 weeks of treatment. These results were in agreement with other study [12], where it was concluded that simvastatin 20 mg/day will significantly reduce serum total cholesterol by 25 % and 22.8% respectively after several weeks of therapy. Further, the results for LDL-C, clearly show a decrease in serum LDL-C by 44.7% this is in conformity with other findings [13,14], where they found a decrease in serum LDL -C by 29.7% and 33.6% by using simvastatin for several weeks. The data in table indicated also that both triglyceride and VLDL-C were significantly reduced after 8 and 16 weeks of treatment. These results were in agreement with that reported earlier.[15,16] they had found that simvastatin 20 mg daily reduce significantly serum triglyceride. The findings concerning VLDL-C, was compatible with a study conducted by other [17], where they found that serum VLDL-C is reduced by 16% after several weeks of treatment by simvastatin. HDL-C, has notably increased by 10.11% after 8 weeks and by 23.6% after 16 weeks of treatment. These results coincided with other studies conducted earlier [18,19], where they noted that treatment by simvastatin 20 mg for several weeks increase the serum HDL-C by 18% and 8.1% . Concerning the atherogenic index, it was significantly reduced as shown in Table (1), which agreed with the findings in another study[18], which showed a decrease by 26.4% after treatment with simvastatin 20 mg. Review of the literature demonstrated controversial effects of simvastatin on hepatic function. Some studies reported an elevations of liver parameters during simvastatin therapy [20], whereas others studies showed that simvastatin has no effect on liver parameters.[21,12] After 16 weeks of treatment, serum ALT, had markedly increased yet within the normal range. Such findings were relevant with other findings[23], which proved that serum ALT, AST and ALP had significantly increased yet within normal ranges after several weeks of therapy by simvastatin 20 mg. Table (2) showed that both total cholesterol and LDL-C were significantly reduced in hyperlipidemic patients treated with atorvastatin 20mg/day after both 8 and 16-weeks of treatment. These results were in agreement with the results presented by other authors [24-27], where they found that atorvastain reduced plasma total cholesterol and LDL-C in patients with hyperlipidemia. As for triglyceride and VLDL-C, they were significantly reduced in hyperlipidemic patients treated with atorvastatin after the 2 intervals of treatment. These results were coincided with a study conducted earlier [28], who found that the daily dose of atorvastatin significantly reduced triglyceride by 31%. Other results [29] did not find a significant decrease in triglyceride after 6 months of treatment by atorvastatin 20 mg daily dose, serum triglyceride baseline was (135 ± 12) mg/dl, after 6 months of treatment was (132 ± 10) mg/dl. It was clearly shown in Table(2) that HDL-C was significantly increased in hyperlipidemic patients, this result was quite similar to that reported by other study [30] , where they found that atorvastatin daily doses significantly increased HDL-C for 12 weeks. Available evidences suggested that the increase in HDL-C with statin therapy results from a combination of increased expression of apoA-I and reduced HDL-C remodeling as a consequence of lowering triglyceride level. [31,32] Atorvastatin treatment

significantly reduced the atherogenic index in hyperlipidemic patients. This result was quite similar to that reported by other [33], where they found that the daily dose of atorvastatin 20 mg for 6 weeks was significantly reduced atherogenic index by 32.3%, while the serum ALT level was significantly increased in hyperlipidemic patients treated with atorvastatin after 8 and 16 weeks of treatment in comparison with the ones before treatment, yet within normal ranges when compared to normal subjects (controls). These results coincided with findings from previous study [34], where they found that atorvastatin 20 mg for several weeks increase ALT from (12 ± 3) as the baseline to (16 ± 6) but they showed that all regimens was well tolerated and none of patients had a significant elevation of liver enzymes (≥ 2 times the baseline). The comparison between the two modes of treatment shows in Table (3) indicates that The mean percent change in total cholesterol was not statistically different between atorvastatin and simvastatin therapy after both 8 and 16-weeks of treatment. The mean percentage changes in triglyceride for atorvastatin group was statistically significant when compared to those of simvastatin after both 8-weeks (- 20.69% VS -10.36%, $p < 0.05$) and 16-weeks of treatment (-31.38% VS 20.35%, $p< 0.05$) these results are in agreement with the study performed earlier [9],who showed that treatment with atorvastatin lower triglyceride more than simvastatin. Reduction of VLDL-C levels in atorvastatin group was statistically significant when compared to those of simvastatin, after both 8- weeks (-19.30% VS -15.25%, $p< 0.05$) and 16-weeks of treatment (-31.58% VS – 25.4%, $p< 0.001$) these results are in consistent with findings from previous study. [32] No statistical difference were observed for LDL-C after 8-weeks of treatment for both drugs. But after 16 weeks of treatment simvastatin shows greater reduction (- 44.7%, $p< 0.05$) than atorvastatine (- 41.22%) and was statistically different. A statistically significant increase in HDL-C was observed after 8-weeks of treatment for atorvastatin than for simvastatin (10.31% VS 10.11%, $p< 0.05$) this result is similar to that reported by other. [9]

Conclusion

After treatment with simvastatin 20 mg and atorvastatin 20mg, there were reductions in total cholesterol, triglyceride, LDL-C, and VLDL-C, and an increase in HDL-C in both groups was observed. Comparing the two modes of treatment after 16-weeks, there were greater decreases in triglyceride and VLDL-C with atorvastatin than with simvastatin while Simvastatin led to greater reduction in LDL-C. Both modes of treatment were well tolerated by the patients.

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