Efficacy and Safety of Fluvastatin Sodium XL 80mg in Treatment of Hypercholesterolemic Patient with Risk Factor of Cardiovascular Disease

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Key words:
Hypercholesterolemia, Dyslipidemia, Lipid lowering agent, Fluvastatin.

Abstract:

Back ground: *Reduction of coronary heart disease (CHD) risk through the modification of risk factors has a strong effect on clinical practice. The introduction of 3-hydroxy-3-methylglutaryl coenzyme-A (HMG-CoA) reductase inhibitors (statins) has significantly advanced the treatment of hypercholesterolemia and in reduction of cardiovascular events and total mortality rates. Among the available statins, Fluvastatin is a newer, synthetic, second generation, potent lipid lowering agent and widely accepted in diverse population. However the safety profile and efficacy was not assessed in Bangladeshi population, a population significantly different from Caucasian population where most studies were done. Current study aimed at evaluating the safety and efficacy of fluvastatin in the specified population.*

Methods: *The study is an open-label, multicenter, quasi experimental study conducted among 162 adult patients suffering from hypercholesterolemia. After through baseline evaluation, the patients were given with Fluvastatin 80 mg once daily for 3 months. All the patients were assessed twice, before and after treatment. Data on demography, of relevant medical history and of physical examination were collected in the both the visit along with data on relevant lipid parameters (Total Cholesterol, LDL-C, HDL-C and TG) were collected at final visit. Safety was assessed by evaluating adverse events, as well as laboratory abnormalities, including liver aminotransferases.*

Results: *Serum total cholesterol was found to be significantly reduced and across two assessments the reduction was 51.2 units (P<.001). Average reduction in LDL-cholesterol was around 40 units (P<.001). Most significant reduction (140.0±305.8 units) was seen in serum LDL cholesterol (P<.001). However; no statistically significant reduction was seen in HLD cholesterol. Safety of fluvastatin was assessed by evaluating the adverse events, as well as through laboratory abnormalities, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Comparison of aminotransferase level was done before and after treatment through paired t test, Neither ALT nor the AST showed statistically significant rise after 3 months treatment of fluvastatin (P>.05). Out of 162 study participant 4.3% had their treatment interrupted, of which 1 (0.62%) had to cease treatment due to lack of efficacy, 1 (0.62%) experienced adverse event, 2 (1.24%) didn't return to follow-up and 3 (1.86%) patients requested their physician to cease the treatment.*

Conclusion: *Three month treatment with Fluvastatin XL 80 mg reduces most of lipid parameter of lipid profile (Total cholesterol, Triglyceride and LDL) significantly. The drug is found to be well tolerated with minimal adverse event during the course of treatment.*

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Introduction:

Atherosclerosis is considered as one the leading cause of death worldwide.[1] The best strategy to decrease the death toll from NCDs such as Atherosclerosis and its consequences is yet to be established in many of the countries concerned. Decisive prevention policies are yet to be formulated and implemented, particularly in resource-limited developing countries. The increased risk of cardiovascular disease is

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associated with an elevated serum cholesterol level[2] and can be reduced by lowering the blood cholesterol concentration[3].

There is now considerable evidence that controlling hypercholesterolemia can reduce the incidence of coronary heart disease.[4] Both non pharmacologic and pharmacologic treatment are in practice. Standard non-pharmacological therapy consists primarily of modification of diet and lifestyle. This therapy may modestly reduce LDL cholesterol, but is not likely to lower the LDL cholesterol level more than about 30 mg/dL.[5] General physicians and heart specialists prescribes the medication in combination with diet and exercise. Pharmacological treatment should be started at an early age in order to prevent premature coronary artery disease. However, the treatment of hypercholesterolemia is occasionally difficult, as moderate hypercholesterolemia gives no symptoms, and the patients often experience side-effects of several chole-sterol-lowering drugs.[6] The ideal drug would be efficacious in lowering plasma lipid levels with no subjective side-effects, would have a documented effect on the clinical endpoint, and would be safe on a long-term basis.[7]

The introduction of HMG-CoA reductase inhibitors (statins) has significantly advanced the treatment of hypercholesterolemia. Statins can reduce LDL cholesterol levels by 20–40% and, at maximum doses; they can lower levels by 40–50%. They also can modestly increase HDL cholesterol levels, usually by about 5–10%. These medications are usually well tolerated, have few side effects.[5]

Published evidence in of recent observations shows the statins as the most commonly used and effective forms of medication for the treatment of elevated cholesterol. The U.S. Preventive Services Task Force estimated that after 5 to 7 years of treatment with statins, the relative risk reduction on coronary heart disease events was achieved by approximately 30%.[8,9] More recently, a systematic review reported an almost identical relative risk reduction of 29.2% in low risk patients treated for 4.3 years.[10] Meta analysis by Bigen et al reported relative risk reduction of 19% in mortality due to coronary heart disease.[11]

From six available statins approved for patients requiring lipid-lowering therapy, Fluvastatin is a preferred one. Among the available statins Fluvastatin is the only synthetic molecule, a second generation, potent competitive inhibitor of 3-hydroxy-3-methylglutaryl coenzyme-A reductase, the rate-limiting enzyme in cholesterol biosynthesis. When used in conjunction with a fat- and cholesterol-restricted diet, it shows marked efficacy in treatment of hypercholesterolemia and mixed hypercholesterolemia.[12] Several clinical outcome trials have shown that substantial benefits are associated with treatment with fluvastatin in diverse populations.

Research in Caucasian population suggests, with its safety profile and evidence of clinical benefits, fluvastatin can play an important role in the treatment of patients with hypercholesterolaemia. Fluvastatin XL has been shown to reduce LDL-cholesterol significantly in high-risk patients to an extent similar to other statins, lovastatin ER, pravastatin and simvastatin at starting dosages, although to a lesser extent than atorvastatin and rosuvastatin.[13]

Because of its safety profile, fluvastatin represent an excellent choice for, patients needing moderate LDL-cholesterol reductions to achieve LDL-cholesterol goals; for patients requiring combination therapy with other lipid-lowering agents; for patients taking multiple medications that place them at high risk for drug interactions during statin therapy; and high-risk patient populations, including patients with renal disease, renal transplantation patients and patients who have undergone coronary intervention procedures.[13] Several clinical outcome trials have shown that substantial benefits are associated with treatment with fluvastatin in such diverse populations. In particular, data from two large, randomised clinical trials[14,15] have demonstrated that fluvastatin is effective for secondary prevention of cardiac events in patients following coronary intervention procedures, and for primary prevention of cardiac events in renal transplant recipients.

However the safety profile and efficacy was not assessed in Bangladeshi population, a population significantly different from Caucasian, Negrito and other racial variations. The aim of the study was to evaluate the safety and efficacy of fluvastatin in the specified population and in its registered indication in treating patients with hyperlipidemia

and or mixed dyslipidemia with risk factors of cardiovascular disease.

Methodology:

Patients and materials:

Current effort is an open-label, multicenter, quasi experimental study conducted among 162 adult patients suffering from hypercholesterolemia to evaluate the safety and efficacy of fluvastatin in Bangladesh population. The study was approved by the institutional review board and was conducted maintaining confidentiality. Initially a total of 169 patients were recruited upon their consent through their treating physician in 40 urban centres of Bangladesh. The assigned physicians were the registered doctors practicing in the urban area. Recruited subjects were adults with registered indication of fluvastatin, having hypercholesterolemia (total cholesterol>200 or LDL≥130mg/dl) and or mixed dyslipidemia with risk factors for Cardiovascular disease, namely, Hypertension (BP≥140/90mm of Hg or on antihypertensive medications), Low HDL-Cholesterol (<40mg/dl), history of recent PCI and Diabetes mellitus. Patients with hypersensitivity to any of the components of fluvastatin, with chronic renal failure (with serum creatinine> 2.0mg/dL), Patient with active liver disease, or unexplained persistent elevations in serum transaminases and pregnant or nursing women were excluded from the study. After thorough baseline evaluation, the patient was given with Fluvastatin 80 mg once daily. To maintain similarity in intervention all the patients were prescribed the investigational drug of same brand (LESCOL XL® sustained release tablet containing 80 mg fluvastatin). To avoid contamination of results, Patients having concomitant therapy with other antihyperlipidemics or drugs with the potential of confounding effect in judgment of the treating physician were dropped. Complete data was not available on 7 patients, as they didn't attend the final follow up assessment. Finally data of 162 subjects, who took the medication for 3 months as prescribed by the physician and attended follow up over the period and of whom complete data was available, were proceeded for final analysis

Assessment of baseline parameters, Outcome and study end points:

All the patients were assessed twice, once at the baseline and once upon completion of three month course of treatment. And the data were recorded in a predesigned Case Report Forms (CRF) by the treating physician. During the first visit, patients were screened for eligibility for enrollment based on the inclusion and exclusion criteria. Baseline data on demography, of relevant medical history and of Physical examination were collected in the visit along with data on relevant lipid parameters revealed through Laboratory investigations (Total Cholesterol, LDL-C, HDL-C and TG). At the end of 3 month therapy the second and final assessment was done repeating the Physical and Laboratory examinations done at baseline for comparison. In the visit additionally data on Safety of the drug was collected by inquiring and recording all adverse events or serious adverse events. An adverse event considered by the treating physician, in the study is any undesirable sign, symptom or medical condition occurring after starting study drug even if the event is not considered to be related to study drug. Information about all adverse events either self reported, or elucidated by the physician were recorded. A Serious adverse event considered for the study is an undesirable sign, symptom or medical condition which is fatal or life-threatening or required prolonged hospitalization or resulted in persistent or significant disability or incapacity or that it may jeopardize the subject and may require medical or surgical intervention.

Statistical analysis:

The data from all 40 centers were pooled and summarized with respect to demographic and baseline characteristics and efficacy and safety observations. Safety was assessed by summarizing frequencies of adverse events and Laboratory evaluation of liver aminotransfares. Adverse events were summarized by presenting the number and percentage of patients having any adverse event. Both post treatment lipid parameters and liver aminotransfares were compared with those of baseline through paired t test. McNemar test is done on 2x2 classification table for comparison of proportion of overweight and hypertension in before after setting. For statistical analysis Statistical software SPSS® version 16[16] and STATA® version 10 I/C[17] were used.

Results:

a. Patient characteristics:

Table-I

Distribution of the study subjects by age and sex

Age group	Male	Female	Total
< 40 years	14 (12.5%)	09 (18.0%)	23 (14.2%)
40 - 49 years	47 (42.0%)	20 (40.0%)	67 (41.4%)
50 - 59 years	38 (33.9%)	11(22.0%)	49 (30.2%)
>= 60 years	13 (11.6%)	10 (20.0%)	23 (14.2%)
Total	112 (100.0%)	50 (100.0%)	162 (100.0%)

Mean age Male 48.7±8.1; Female 48.7±10.2

Table 1 shows the distribution of the study participants by age and sex. Out of 162 participants 112 (69.1%) were male and 50 (30.9%) were male. Mean age among Male was 48.7±8.1 year and among Female was 48.7±10.2 year. Among the study participants 14.2% were aged below 40 years, 41.4% were aged between 40–49 years, 30.2% were aged between 50 – 59 years and 14.2% were aged above 60 years.

Number in parenthesis indicated column percentage, *Statistically significant at P<.05, McNemar test is done on 2x2 classification table for comparison of proportion in before after setting.

Anthropometric measurements were recorded and BMI was calculated from height and weight recorded both at baseline and after treatment. Majority of the (82.1%) participants were overweight at baseline and at the 2nd visit the

Table-II

Comparison of BMI and Hypertension status before and after treatment

Variables	Assessment time		Paired difference		
	Visit 1	Visit 2	proportions	95% CI	p value
BMI Category					
Normal weight(d" 24)	29 (17.9%)	37 (22.8%)	4.94%	-0.5% to 8.4%	0.077
Over weight (>24)	133(82.1%)	125 (77.2%)			
Hypertension					
Yes	100 (61.7%)	152 (93.8%)	32.10%	26.1% to 32.7%	0.001*
No	62	(38.3%)	10 (6.2%)		

Table-III

Distribution of the study subjects by history of medical condition and concomitant medication (n=162)

Variables	Frequency	Percent
Medical condition		
Yes	50	30.9
No	112	69.1
Concomitant medication		
Yes	53	32.7
No	109	67.3

Table-IV

Comparison of lipid profile before and after fluvastatin treatment through paired t test

Variables	Assessment time		Paired mean difference		
	Visit 1	Visit 2	Difference	t Value	p Value
Total cholesterol (n=162)	269.9±57.3	218.1±40.6	51.9± 34.8	18.94	.000*
Triglyceride(n=162)	400.0±337.9	260.4±115.5	140.0±305.8	05.83	.000*
LDL (n=162)	161.1±54.5	121.1±33.2	40.1± 48.0	10.62	.000*
HDL(n=162)	42.3±45.8	42.11±25.5	0.17± 37.6	00.06	.953

* Statistically significant; p value was generated through paired t test.

Table-V

Comparison of aminotransferase before and after fluvastatin treatment through paired t test

Variables	Assessment time		Paired mean difference		
	Visit 1	Visit 2	difference	T value	p value
ALT	33.52±9.3	33.10±8.0	.425±5.119	0.53	.602
AST	26.79±8.3	25.21±7.2	1.583±4.127	1.88	.073

Table-VI

Outcome assessment of treatment

	Variables	Frequency	Percent
1	Interruption of treatment		
	Yes	07	4.3
	No	155	95.7
	Total	162	100.0
2	Reason for interruption		
	Lack of efficiency	01	14.3
	Adverse event	01	14.3
	Patient's request	03	42.9
	Lost to follow up	02	28.6
3	Tolerance		
	Very good	95	58.6
	Good	67	41.4
4	Success		
	Very good	91	56.2
	good	68	42.0
	Not satisfactory	03	1.9

proportion of overweight was reduced to 77.2%, however the decrease was not statistically significant (P>.05). Blood pressure was measured at both the assessment, A systolic BP>140 mmHg or diastolic BP>90 mmHg was considered as hypertension. At the commencement of the study the proportion of hypertension measured was 38.3% and at the 2nd visit the proportion dropped sharply to 6.2% and the decrease was highly significant (P<.01).

Table shows the distribution of the study subjects by presence of medical condition at base line and concomitant treatment during the drug therapy. Among the patients 30.9% had been suffering from any medical condition and 32.7% received concomitant medication while taking fluvastatin therapy.

b. Efficacy of Fluvastatin

Efficacy of fluvastatin treatment was assessed by assessing the lipid lowering capability of the drug by comparing after-treatment lipid profile with the baseline. The mean of difference in total cholesterol across two assessments was 51.19 mg/dl. Statistical operation suggests significant decrease in total cholesterol level with the treatment (P<.001). Similar decreasing trend is seen in serum triglyceride (P<.001) and LDL cholesterol (P<.001). However HDL cholesterol remained similar across two measurements. (p >.05)

C. Safety of fluvastatin

Safety profile of fluvastatin treatment was assessed by comparing aminotransferase before and after fluvastatin treatment through paired t test, with a view to assess the risk for reversible elevation of liver transaminases. Neither Alanine aminotransferase (ALT) nor the Aspartate aminotransferase (AST) showed statistically significant rise after 3 months treatment of fluvastatin (p>.05).

Safety of the treatment was assessed based primarily the opinion of the physician concerned. A total 7(4.3%) of the total 162 participant had their treatment interrupted. Among the seven patients with interrupted treatment 1 (14.3%) had to cease treatment due to lack of efficacy, 1 (14.3%) experienced adverse event, 2 didn't return to follow-up and 3 (42.9%) patients requested their physician to cease.

Discussion:

Among the available statins, Fluvastatin is the only synthetic molecule, a second generation, potent competitive inhibitor of 3-hydroxy-3-methylglutaryl coenzyme-A reductase, the rate-limiting enzyme in cholesterol biosynthesis. and has emerged as an effective therapeutic option for treatment of elevated cholesterol levels[3] which in turn contribute to the reduction of major coronary events and death in a wide range of individuals at risk for these events.

Mounting evidence from randomized clinical trials with statins has shown significant reduction in the incidence of CHD.[18,19,20] These Trials were conducted with different available statins and demonstrated statistically significant beneficial effect on reducing cholesterol level as well the reduction of incidence of mortality and morbidity from wide range of cardiovascular causes. Systematic review of RCT by LaRosa[21] also substantiated the efficacy of statins as reducer of cholesterol level eventually as a cardio protective agent. In their study pooled analysis of around 30,000 patients' data revealed evidence of 28% reduction in LDL-cholesterol, 31% reduction of coronary events and 29% of death due to coronary heart disease. Apart from coronary heart disease a significant reduction in stroke was also reported in major clinical trials with statins in the review.

When used in conjunction with a fat- and cholesterol-restricted diet, it shows marked efficacy in treatment of hypercholesterolemia and mixed hypercholesterolemia.[22] Several clinical outcome trials have also shown that substantial benefits are associated with treatment with fluvastatin in diverse populations.

Its safety profile and efficacy was not assessed in Bangladeshi population, a population significantly different from Caucasian, Negrito and other racial variations. Authors intension was to evaluate the safety and efficacy of fluvastatin in the specified population and in its registered indication in treating patients with hyperlipidemia and or mixed dyslipidemia with risk factors of cardiovascular disease in Bangladesh population.

Participants were treated with Fluvastatin 80 mg once daily. Among the different formulations available in the market Fluvastatin XL 80 mg once daily was chosen and interventional regimen. Different formulations of fluvastatin available in the market have shown nonlinear pharmacokinetics at doses of greater than 20 mg.[23,24] Consequently, there are greater than expected systemic drug concentrations in patients receiving higher doses of fluvastatin, which may lead to increased risk of adverse events, and in particular, of dose-related musculoskeletal and hepatic toxicities that are associated with this class of drugs. The greater-than-expected increase in systemic bioavailability at high doses may be due to saturable first-pass hepatic metabolism of fluvastatin.[25] Increasing the duration of hepatic exposure to fluvastatin through slower delivery may decrease the systemic drug levels, which may improve tolerability at higher doses while maintaining the drug's dose-ordered efficacy. Hence , extended-release matrix tablet formulation of fluvastatin 80 mg has been chosen to ensure sustained release of fluvastatin over 8–12 h, resulting in lower systemic drug levels as proposed by Ballantyne, McKenney and Trippe. [26]

All the patients were assessed twice, once at the baseline and once upon completion of three month course of treatment. Of the 162 patients enrolled in the study, around seventy percent were male and more than seventy percent were aged between 40–59 years. With a view to estimate the cardiovascular risk reduction adult subjects with registered indication of fluvastatin, e.g. patient having hypercholesterolemia and or mixed dyslipidemia with risk factors for cardiovascular disease, namely, Hypertension, Low HDL Cholesterol, history of recent PCI and Diabetes mellitus were recruited.

Majority of the participants were overweight at baseline and at the 2nd visit the subtle decrease in the proportion of overweight was found. At baseline four out of every five of the study participants were overweight and at the end of treatment the proportion was 77.2%. Paired comparison of pre and Post treatment BMI was performed through paired t test. On average only 0.41 kg/m^2 reduction of BMI was found with the treatment which was neither statistically significant nor clinically relevant. Evidence doesn't suggest Fluvastatin as a weight reducing agent; probably this is the rationale for employing concomitant lifestyle modification and physical exercise along with lipid lowering therapy. General physicians and cardiologists prescribe the medication in combination with diet and exercise.

Blood pressure was measured at both the assessment, A systolic BP>140 mmHg or diastolic BP>90 mmHg was considered as hypertension. At the commencement of the study the proportion of hypertension measured was 38.3% and at the 2nd visit the proportion dropped sharply to 6.2% and the decrease was found to be highly significant (P<.01). High prevalence of hypertension among

hypercholesterolemic patients is not surprising, it would rather support a plausible explanation co-existence of several metabolic disease like diabetes, Obesity, hypertension etc. in patient of metabolic syndrome.

Even sharp reduction in the proportion of hypertension doesn't necessarily denote the anti-hypertensive effect of Fluvastatin, reason for such decrease would be the concomitant use of antihypertensive. Patient diagnosed as hypertensive by the physician at baseline, were rationally prescribed necessary antihypertensive along with the lipid lowering agent. Although, to avoid contamination of results, Patients having concomitant therapy with other anti-hyperlipidemics or drugs with the potential of confounding effect in judgment of the treating physician were dropped. However the use of antihypertensive was not prohibited.

Efficacy of fluvastatin treatment was assessed by assessing the lipid lowering capability of the drug by comparing after treatment lipid profile with the baseline. Serum total cholesterol was found to be significantly reduced and across two assessments the reduction was 51.2 units. Average reduction in LDL-cholesterol was around 40 units. Most significant reduction was seen in serum LDL cholesterol (140.0±305.8). However, No statistically significant reduction was seen in HLD cholesterol.

n study by Langtry et al[27] fluvastatin has been shown to decrease serum LDL-C, total cholesterol and triglyceride levels, and to elevate HDL-C. However in our study the level of HDL-cholesterol remained static. Another similar study like ours[28] evaluated the effects of fluvastatin XL 80mg on the lipid profile and showed statistically significant improvement with fluvastatin treatment in mean total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglyceride values over the duration 3 and 6 months. Although our study only could reveal treatment efficacy of 3 month duration, the Di Lullo[28] study confirms the lipid lowering effect of relatively longer duration, which justifies effect of longer duration of treatment. A prospective study of wider time span could elucidate further evidence.

Although fluvastatin exerts effect on all three bad cholesterol, most study highlighted its effect on LDL-cholesterol. Zavoral et al. [29]demonstrated in a long-term, open-label study that fluvastatin lowered LDL-C by 25% to 31%. In a pooled analysis[30] of data of three RCT showed that LDL-C-lowering effect of fluvastatin was apparent after 2 weeks of treatment, and the full effect was observed within 4 weeks of treatment initiation. After 4 weeks of treatment with fluvastatin XL 80 mg HS, LDL-C levels were reduced by a mean of 36.3%.

Fluvastatin inhibits the progression of lesions in the coronary arteries, as evidenced by the Lipoprotein and Coronary Atherosclerosis Study (LCAS),[31] the Fluvastatin Angiographic Restenosis (FLARE)[32] and the Lescol in Symptomatic Angina (LISA)[33] trials. Therefore, it has been shown that fluvastatin is beneficial in the secondary prevention of coronary atherosclerosis. More recently, März et al.[34] showed that fluvastatin causes a shift in LDL-C subfractions toward more buoyant, less atherogenic LDL particles in post-menopausal women with combined hyperlipidemia both in primary and in secondary prevention. This may explain the greater antiatherogenic effect of fluvastatin than expected based on changes in serum lipids alone.

Tolerability was assessed by evaluating new and worsening adverse events, as well as laboratory abnormalities, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Comparison of aminotransferase level was done before and after fluvastatin treatment through paired t test, with a view to assess the risk for reversible elevation of liver transaminases. Neither Alanine aminotransferase (ALT) nor the Aspartate aminotransferase (AST) showed statistically significant rise after 3 months treatment of fluvastatin.(P>.05). The result suggests no significant liver enzyme increase in the study participants, although elevation of liver aminotransferase has been considered as an adverse effect of statin therapy and this has been recorded as a contraindication of such drugs. However study by Ballantyn[30] also didn't notice an increase in ALT or AST.

Evaluation of adverse event of the treatment was assessed based on the opinion of the physician

concerned. A potential limitation of our study was that for safety data we had to depend on the turnout of patient at final follow-up. However in the current study only 7(4.1%) patient were excluded due to incompleteness of data or loss to follow-up before deciding final sample. The figure was not bigger enough to impede the generalizability of study finding. At final follow-up, in addition to repetition of the baseline parameters and laboratory investigations, data on Safety of the drug was collected by inquiring and recording all adverse events or serious adverse events. According to our data out of 162 study participant 4.3% had their treatment interrupted, of which 1 (0.62%) had to cease treatment due to lack of efficacy, 1 (0.62%) experienced adverse event, 2 (1.24%) didn't return to follow-up and 3 (1.86%) patients requested their physician to cease the treatment. Several studies[28,30] also showed fluvastatin treatment as effective in improving the lipid profile, and it demonstrates good safety and tolerability. A systematic review by Corsini et al [13] concluded based on recent data from several clinical outcome trials that substantial benefits are associated with treatment with fluvastatin in diverse populations. They also suggested a strong benefit-to-risk profile for fluvastatin.

Our study confirms/ maintains similar stance to the fluvastatin treatment as lipid lowering modality as revelled in other population. Current study validates the use of fluvastatin XL 80mg once daily as an effective and safe lipid lowering treatment for reduction of adverse cardiac events. Current study is a quasi experimental study, not randomized, which to some extent limits generalizability of the findings, however, the intension of the researcher was to assess the safety and efficacy of the study in our population which was already recommended by large, well designed and well powered studies elsewhere in wide range of population and patient settings. Further investigation could be done preferably a phase III or IV RCT for even stronger evidences.

Conclusion:

Three month treatment with Fluvastatin XL 80 mg reduces most of lipid parameter of lipid profile (Total cholesterol, Triglyceride and LDL) significantly. However no significant change in HDL is demonstrated with the treatment. Although treatment with statins are said to pose risk of raising liver enzyme , current data didn't find any excess risk of increasing liver enzymes. The drug is found to be well tolerated with minimal adverse event during the course of treatment. However the drug doesn't seem to be effective in weight reduction as BMI remains almost similar in two measurements.

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