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Original Research Article

Assessing the Impact of Body Mass Index on Lipid Lowering Treatment Choice: Fenofibrate vs. Atorvastatin in Atherogenic Dyslipidemia Patients

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Abstract:

The impact of Body Mass Index (BMI) on the choice between Fenofibrate and Atorvastatin as treatments for patients with atherogenic dyslipidemia (AD). A total of 156 patients with AD were split into two groups, one receiving Atorvastatin and the other receiving Fenofibrate for a period of three months. The initial results indicated that BMI plays a significant role in the decision of which lipid-lowering treatment to use for patients with AD. An analysis of the lipid profile among different BMI categories revealed that atorvastatin was effective in reducing LDL-C, TC, and TG levels, while fenofibrate was more effective in improving HDL-C and reducing TG levels in AD patients. After the three-month period, it was found that atorvastatin was more successful in lowering the lipid profile (TC, TG, and LDL-C) compared to fenofibrate. A positive relationship was identified between higher BMI and the preference for fenofibrate over atorvastatin. Furthermore, patients who were classified as obese or overweight showed better responses to fenofibrate compared to atorvastatin, resulting in improved lipid profiles. It is essential for healthcare providers to consider BMI when determining the appropriate lipid-lowering medication for patients with AD. Additional research is needed to confirm and expand upon the results of this study.

Keywords: Atorvastatin; Fenofibrate, BMI, Atherogenic Dyslipidemia; Lipid Profile.

Introduction

Atherogenic Dyslipidemia (AD) refers to a condition marked by increased levels of triglycerides (TG) and decreased levels of high-density lipoprotein cholesterol (HDL-C), and it poses a notable threat to cardiovascular health [1]. The body mass index (BMI) plays a pivotal role in determining the strategies for the treating high level of fats in the blood [2]. BMI has been linked to a higher chance of developing cardiovascular problems and an increased risk of death from any cause. Numerous studies have examined the connection between BMI and specific components of serum lipids [2-3]. Current guidelines for the management of dyslipidemia prioritize the reduction of LDL cholesterol (LDL-C) levels [4]. These guidelines offer specific target levels tailored to each risk group to effectively mitigate cardiovascular risks. The European Atherosclerosis Society and the National Cholesterol Education Programme (NCEP) acknowledge fibric acid derivatives (Fibrates) and Hydroxy Methylglutaryl CoA reductase inhibitors (HMG CoA reductase inhibitors) as suitable treatments for AD [5]. Among these, Statins (HMG CoA reductase inhibitors) have proven to be the most efficacious and well-tolerated medications for managing hypercholesterolemia.

Many different medications have proven to be effective in treating AD, a condition characterized by abnormal lipid levels. Among these medications are fenofibrate and atorvastatin. However, there is still uncertainty regarding the influence of body mass index (BMI) on the decision to choose between these two treatment options. The purpose of this study is to investigate the correlation between BMI and the selection of either fenofibrate or atorvastatin as a lipid-lowering treatment for North Indian patients with AD.

Material and Methods

The present study was conducted in the Department of Physiology & Department of Pharmacology, attending the OPD patients of the Medicine at Rajashri Dashrath Autonomous State Medical College Ayodhya (U.P.), India. Ethical clearance was taken by Institutional Ethic Committee. Based on the parameters of a 2-sided level of statistical significance of 0.05; 80% power, and a between group difference of responders by 100%, the

sample size was calculated. Consequently, each treatment group was found to require 78 subjects.

Selection of Subjects:

The eligible subjects were instructed to follow a standard diet that helps lower lipid levels for a month before their baseline blood analysis. After this phase, they were randomly divided into two groups. One group received a daily dose of 10 mg tab of Atorvastatin, while the other group received a daily dose of 200 mg tab of micronized Fenofibrate. Follow-up visits were scheduled at the 1st and 3rd month, during which the cases underwent clinical assessments, blood investigation, and evaluations of their adherence to the treatment regimen. In the atorvastatin group, the dose of the drug was gradually increased at each visit, reaching up to 80 mg per day if the levels of LDL-C (low-density lipoprotein cholesterol) did not decrease below 130 mg/dL (or below 100 mg/dL for patients with coronary or cerebrovascular disease). On the other hand, the dosage of fenofibrate remain unchanged throughout the treatment period for the participants in the fenofibrate group [6].

Inclusion Criteria:

1. Men and women 35 to 74 years of age with mixed Atherogenic Dyslipidemia (triglycerides, > or = to 150 mg/dL to < 400 mg/dL; HDL-C < 40 mg/dL for males, < 50 mg/dL for females; LDL-C, > or = to 130 mg/dL).
2. Subjects must agree to use for serum lipid reference level, National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) guideline was referred.

Exclusion Criteria:

1. Subjects with unstable or uncontrolled medical conditions considered inappropriate in a clinical trial.
2. Subjects with an unstable dose of medications or receiving Coumadin, oral, intravenous, or intramuscular cyclosporine.
3. Women who are pregnant or plan on becoming pregnant, or women who are lactating.

To assess compliance with the prescribed medications, the researchers counted the number of pills returned by the patients and calculated the percentage of pills taken compared to the number of scheduled doses. We have considered all patients for this analysis, considering the following available parameters: body weight, height, total cholesterol (TC), LDL-C, HDL-C, and triglycerides (TG). All the parameters were done by standard protocol [7-8].

Statistical Analysis

The data obtained from the research was analyzed using various statistical techniques. To check the normality of continuous data, the Kolmogorov-Smirnov test was employed. On the other hand, categorical data was presented in terms of frequency and percentage. The representation of continuous data was done using the mean and standard deviation. The study utilized either Pearson (for parametric) or Spearman's (for non-parametric data) correlation coefficient to determine the correlation between BMI and lipid profile data. Additionally, an ANOVA post hoc Least Significant Difference (LSD) test was employed to identify any significant differences between BMI and individual lipid profile levels. Z test was used for comparation between selected two drug group. For the statistical analysis, the software package used was the Statistical Package for the Social Sciences (SPSS-21) by IBM, located in Chicago, USA. Additionally, the graphs illustrating the data were created using Prizm software. To determine the significance of the results, a two-tailed p-value of less than 0.05 was considered significant.

Results

A total of 156 individuals diagnosed with Atherogenic Dyslipidemia (AD) were participating in the study. Among them, a small portion of 1.2% were categorized as underweight, having a body mass index (BMI) below 18.5 kg/m^2. Approximately 31.4% of the participants had a normal weight, falling within the BMI range of 18-25 kg/m^2. The majority, constituting 42.3% of the subjects, were classified as overweight based on their BMI falling within the range of greater than 25-30 kg/m^2. Within the remaining participants, 16.6% exhibited class I obesity (BMI greater than 30-35 kg/m^2), 5.1% displayed class II obesity (BMI greater than 35-40 kg/m^2), and the remaining 3% were classified under class III obesity (BMI greater than

40 kg/m^2) (Table 1). In this study, it was determined that gender did not have a significant impact ($p>0.05$).

Table 1: Baseline characteristics of study subjects

Parameters	BMI <25 [N=51]	BMI 25-30 [N=66]	BMI 30-35 [N=26]	BMI >35 [N=13]	Total [N=156]	p value
Age (Mean±SD)	62.83±8.45	60.97±9.74	58.66±7.64	57.61±7.46	60.02±8.01	<0.01
BMI (kg/m^2)	23.43	28.91	31.80	36.80	30.24	<0.001

Female (N, %)	21 (41.2)	29 (43.9)	8 (30.7)	6 (46.1)	64 (41.02)	0.68
Male (N, %)	30 (58.8)	37 (56.1)	18 (69.2)	7 (53.8)	92 (58.9)	
SBP (mm Hg)	131.37±14.51	133.57±14.71	136.10±15.41	137.20±14.66	134.56±14.84	<0.01
DBP (mm Hg)	77.13±8.94	79.16±9.74	80.19±10.43	81.05±11.71	79.38±9.45	<0.01
Hypertention (N, %)	31 (60.7)	43 (65.2)	20 (76.9)	11 (84.6)	105 (67.3)	<0.01
Diabetes (N, %)	16 (31.4)	25 (37.8)	14 (53.8)	8 (61.5)	63 (40.4)	<0.001
heart disease (N, %)	6 (11.8)	8 (12.1)	4 (15.4)	2 (15.4)	20 (12.8)	<0.01
peripheral artery disease (N, %)	3 (5.88)	4 (6.1)	4 (15.4)	2 (15.4)	13 (8.33)	<0.01
lipid profile (mg/dl)						
LDL-C	98.49±18.94	99.73±19.71	100.76±18.11	99.46±20.48	99.61±18.43	0.45
HDL-c	51.64±11.13	47.92±12.75	44.15±5.77	46.44±5.61	48.04±8.43	<0.031
TC	221.0±25.49	233.12±24.82	238.50±26.93	230.64±25.55	228.82±25.58	<0.018
TG	180.42±26.11	188.61±24.58	197.46±25.84	199.35±25.94	182.71±25.59	<0.05

SBP: systolic blood pressure, DBP: diastolic blood pressure

The occurrence of high blood pressure and hypertension are more common in individuals with higher BMI levels, with a peak of 84.6% in patients with a BMI over 35 kg/m^2. Similarly, the prevalence of diabetes also escalates with increasing BMI, starting at 31.4% in patients with a BMI below 25 kg/m^2, and rising to 37.8% in those with a BMI of 25 to 30 kg/m^2, 53.8% in individuals with a BMI of 30 to less than 35 kg/m^2, and reaching 40% in those with a BMI of >35 kg/m^2. Additionally, the likelihood of heart disease and peripheral artery disease increases as BMI category goes up (Table 1).

In the analysis of patients' lipid profiles, it was observed that there was no significant difference in LDL-C levels across different BMI subcategories (p=0.45). However, HDL-C levels exhibit an inverse relationship with various categories of BMI. Specifically, the values were recorded as 51.64±11.13, 47.9±12.7, 44.1±4.7, and 48.1±8.4 mg/dl for the <25, 25-30, 30-35 and >35 BMI kg/m^2 group, respectively. TC and TG levels were also showed an increase with higher BMI. The average atorvastatin dose for overall population was 15.22±11.83 mg/day. The daily doses increased with increasing BMI. Upon conducting a post hoc analysis of the lipid profile among different BMI subcategories, it was observed that atorvastatin demonstrated greater efficiency in reducing LDL-C, TC and TG levels in patients, while Fenofibrate effectively improved HDL-C and reduces TC levels in patients (Table 2).

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Table 2: Comparison between Atorvastatin verses Fenofibrate group

	Group 1: Atorvastatin (N=78)					Group 2: Fenofibrate (N=78)				
		LDL-C$	HDL-c!	TC¥	TG€		LDL-C$	HDL-c!	TC¥	TG€
BMI <25	Base line	86.6^{a}± 15.6	51.5^{a}± 10.7	215.3^{a} ±43.1	168.8^{a}± 89.3	Base line	86.6 ^{a} ±13.4	51.5^{a}±10.7	215.3^{a}±43.1	168.8^{a}±89.3
	1st M	60.3^{b}± 13.1	52.6^{a}± 11.2	163.7^{b} ±34.4	120.6^{b}± 66.8	1st M	76.5^{b} ±13.8**	56.2^{b}±16.3*	188.4^{b}±34.3**	133.7^{b}±60.1*
	3rd M	55.7^{c}± 10.5	54.6^{a}± 13.4	158.8^{c,b} ±30.7	103^{c} ±56.6	3rd M	75.3^{b,c}±10.5**	60^{c}±14.5**	167.4^{c}±30.2*	110.6^{c,b} ±58.7*
BMI 25-30	Base line	88.9^{a}± 14.7	46.7^{a}± 9.6	222.9^{a} ±39.9	175.6^{a}± 85.2	Base line	88.9^{a}±15.9	46.7^{a}±9.6	222.9^{a}±39.9	175.6^{a}±85.2
	1st M	59.7^{b}± 12.6	49.6^{a}± 14.3	160.2^{b} ±33.2	128.3^{b}± 59.1	1st M	81.1^{b}±14.7**	51.3^{b}±10.2	202.8^{b}±40.1**	130.7^{b} ±73.4
	3rd M	54^{b}±12.8	52.7^{b}± 15.1	156.9^{c,b} ±28.1	111.4^{c}± 63.5	3rd M	79.3^{b,c}±14.1**	57.6^{c}±15.5**	198.6^{b,c}± 35.3**	118.4^{c,b}± 56.7
BMI 30-35	Base line	94.6^{a}± 13.2	45.6^{a}± 10.7	228.7^{a} ±41.3	180.2^{a}± 96.7	Base line	94.6^{a}±15.2	45.6^{a}±10.7	228.7^{a}±41.3	180.2^{a}±96.7
	1st M	70.1^{b}± 12.8	46.7^{a}± 15.2	170.6^{b} ±26.6	130.3^{b}± 70.6	1st M	90.3^{a,b}±15.9**	49.3^{b}±13.7*	198.6^{b}±34.4*	150.3^{b}±80.4*
	3rd M	63.4^{c} ±9.7	47.2^{b}± 15.8	153.9^{c} ±23.4	106.7^{c}± 50.3	3rd M	86.6^{c,b}±14.2**	56.4^{c}±15.9**	197.6^{b,c}± 35.9**	130.7^{c,b}± 63.1*
BMI >35	Base line	95.7^{a}± 14.1	45.1^{a}± 11.3	231.5^{a} ±40.5	186.5^{a}± 95.5	Base line	95.7^{a}±14.9	45.1^{a}±11.3	231.5^{a}±40.5	186.5^{a}±95.5
	1st M	73.4^{b}± 10.8	47.9^{a,b} ±13.7	186.9^{b} ±37.1	123.6^{b}± 55.8	1st M	87.6^{b}±14.2*	49.2^{b}±14.5*	202.4^{b}±42.3**	155.8^{b}±74.9*
	3rd M	65.6^{c}± 8.4	58.1^{b}± 13.8	160.9^{c} ±20.4	118.7^{c,b} ±56.4	3rd M	86.4^{c,b}±13.6**	59.7^{c}±16.2**	195.6^{c,b}± 36.4**	153.1^{c,b}± 76.3**

1st M: 1st month; 3rd M: 3rd month; Significance of individual lipid profiles in relation to subcategory of BMI was assessed by LSD, ANOVA at p:0.05; dissimilar alphabets show significant variation; symbol $: used for LDL-C; !: for HDL; ¥ : For TC and € : TG for Comparison between Atro Vs Fen group. *: p<0.05. **: p<0.01.

In this research, a different statistical analysis was conducted comparing individual lipid profile of between selected drug groups. The findings show that Atorvastatin LDL-C decreases by 35.6%, 39%, 32.9%, and 31.4%, while Fenofibrate decreases by 13%, 10.7%, 8%, and 9% in the BMI subcategory <25, 25 to 30, 30 to 35 and > 35, respectively (Figure 1).

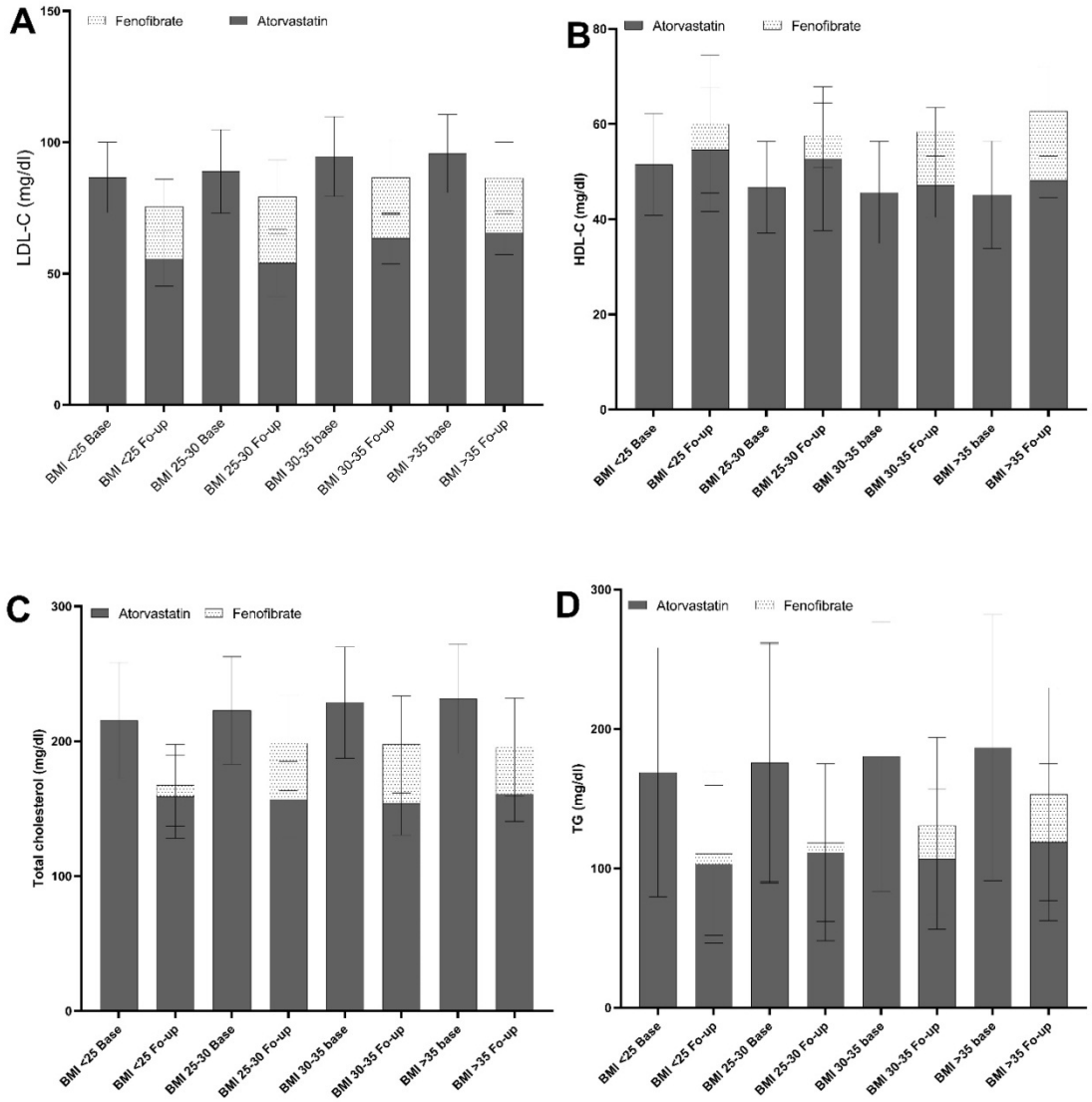

Figure 1: Distribution of lipid profile in comparison with BMI

After three months of follow-up, it was observed that Atorvastatin was more effective in reducing the lipid profile (TC, TG and LDL-C) compared to Fenofibrate. On the other hand, Fenofibrate demonstrated greater efficacy in managing HDL-C levels compared to Atorvastatin in AD patients. There was no significant correlation between LDL-C and TC levels with BMI ($p>0.05$). However, HDL-C showed a negative correlation, while TG showed a positive correlation with BMI ($p<0.05$) (Table 3).

Table 3: Correlation table of lipid profile with Body mass index (BMI)

Lipid profile (mg/dl)	BMI (kg/m^2)	P value
LDL-C	R^2=0.03	0.49
HDL-c	R^2=-0.23	0.001*
TC	R^2=0.04	0.61
Triglyceride	R^2=0.27	0.03*

In the present study, the BMI affects the choice of lipid-lowering medications for individuals with Atherogenic Dyslipidemia (AD), focusing on the comparison between Fenofibrate and Atorvastatin. The study revealed a correlation between BMI and HDL-C and triglyceride levels, but not with LDL-C. Consistent with previous research, the results showed that higher BMI was associated with lower

HDL-C levels and higher triglyceride levels [9-10]. However, we did not observe any significant relationship between BMI and both total cholesterol levels and LDL-C. In this study, a total of 156 AD patients were randomly assigned to two groups: one receiving Atorvastatin and the other receiving Fenofibrate. Both groups had an equal number of participants. Atorvastatin is commonly prescribed for treating high cholesterol levels [10]. Research has consistently shown that this medication reduces the risk of heart-related issues by lowering levels of LDL cholesterol in the blood when combined with PCSK9 inhibitors [11-12]. In medical settings, when patients have common cardiovascular risk factors like diabetes and hypertension, it is more likely that their healthcare provider will recommend Atorvastatin therapy [13]. Furthermore, a high BMI has also been associated with the use of Atorvastatin [14].

In this study, we found that BMI positively associated atorvastatin dose. Atorvastatin was found to be more effective than Fenofibrate in lowering LDL-C levels in AD patients with a BMI between 25 to 30. On other hand, fenofibrate was more effective in high BMI. The study revealed that after three months of monitoring, atorvastatin showed superior results in improving the lipid profile, including total cholesterol (TC), triglycerides (TG), and LDL-C, when compared to Fenofibrate in lower or moderate BMI [10]. This outcome aligns with existing literature, with some researchers suggesting that atorvastatin works by reducing cholesterol in liver cells and enhancing the LDL reducing pathway [6].

Contrastingly, Fenofibrate exhibited better outcomes in raising HDL-C levels in AD patients compared to Atorvastatin. The results indicate that Fenofibrate boosts HDL-C levels by 14.2%, 18.9%, 21.9%, and 28.1%, while Atorvastatin increases them by 5.6%, 11%, 3%, and 6.2% in the BMI subcategory <25, 25 to 30, 30 to 35 and > 35, respectively. This finding clearly showed that atorvastatin was not effective in managing HDL-C levels in AD patients with higher BMI when compared to the usage of atorvastatin. On other hand, there was no significant association between LDL-C and TC levels with BMI, but HDL-C displayed a negative correlation while TG showed a positive correlation with BMI ($p<0.05$). Previous studies, Atorvastatin was shown to be more effective than Fenofibrate in increasing HDL-C levels, decrease level of TG & LDL-C offering a potential advantage in the treatment of AD patients [15]. Nevertheless, a lingering query remains regarding whether the increase in high-density lipoprotein (HDL) relative to low-density lipoprotein (LDL) levels could potentially heighten the risk for patients with AD [6, 16]. Numerous prominent studies on preventive measures have shown that the use of fibrates to elevate HDL cholesterol (HDL-C) levels significantly decreases the progression of cardiovascular events and atherogenic dyslipidemia [6, 11, 16]. Recent analyses of certain trials have suggested that boosting HDL-C in individuals with consistently elevated LDL levels may only offer limited advantages in managing AD patients [17-18].

Conclusion

Both Lipid Lowering Treatment Choice significantly improved the lipid profile; it is evident that Atorvastatin is superior to fenofibrate in achieving the desired lipid levels in patients with AD. Therefore, Atorvastatin could be considered as the preferred medication for treating AD patients with low or moderate BMI in improving Efficacy in higher serum HDL-C and lowering serum TC, TG & LDL. However, the potential benefits of fenofibrate in improving HDL-C metabolism at higher, and reducing TG levels in BMI in AD patients need to be further explored in a larger study to determine if it can lead to clinical advantages.

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