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Dr. Sachin Ambirwar Pundlikrao
Associate Professor, Department of Pharmacology, Sree Lakshmi Narayana Institute of Medical Sciences, Puducherry, India

Dr. Haripriya Uppala
Assistant Professor, Department of Pharmacology, Sree Lakshmi Narayana Institute of Medical Sciences, Puducherry, India

Corresponding Author:
Dr. Haripriya Uppala
Assistant Professor, Department of Pharmacology, Sree Lakshmi Narayana Institute of Medical Sciences, Puducherry, India

To study the impact of biotin on dyslipidemia

Dr. Sachin Ambirwar Pundlikrao and Dr. Haripriya Uppala

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Abstract
Introduction: Dyslipidemias are a growing problem in world health, but patients often go undiagnosed and untreated. The researchers in this study wanted to see how much of a difference taking 20 mg of Atorvastatin daily with 5 mg of biotin daily made in terms of the percentage change from baseline in lipid parameters at weeks compared to the control group.
Methods: Following the acquisition of written informed consent, 50 patients with secondary dyslipidemia and ages 45 to 60 were included. This study was conducted at the Department of Pharmacology, Shree Lakshmi Narayana Institute of Medical Sciences Pudduchery, India between March 2019 to February 2020. They were randomly assigned to one of two groups after completing baseline laboratory examinations and lipid profiles. Those who served as controls. Received Atorvastatin 20 mg alone and the study group received Biotin 5mg combined with Atorvastatin 20 mg for 6 weeks. Twelve weeks of follow-up were conducted with both groups.
Results: At 6 weeks, total cholesterol, LDL cholesterol, triglycerides, and very low density lipoprotein (VLDL) were all lower with combination therapy than with monotherapy. There was no statistically significant difference between the groups when Biotin was added, however HDL levels rose even more. Optimal levels of total cholesterol to HDL were achieved in the combination group, where the ratio reached 3.54. Combined treatment also reduced adverse events.
Conclusion: When compared to Atorvastatin alone, the efficacy of a combination therapy involving 5 mg of biotin and 20 mg of atorvastatin in lowering total cholesterol, LDL cholesterol, and triglycerides is significantly higher. When used as an adjuvant hypolipidemic medication in cases of secondary dyslipidemia, biotin is both safe and well-tolerated.

Keywords: Fibrates, statins, biotin, lipid profile, and creatine kinase

Introduction
Complications from dyslipidemias are quickly becoming a major issue in public health around the world. By 2020, 2.6 million people in India would lose their lives to cardiovascular illnesses, which are a direct result of dyslipidemias. This makes it one of the leading causes of disability and death in developing nations [1, 2].
There is no denying the critical role that these lipoprotein abnormalities play in the development and progression of atherosclerosis, as well as in the high rates of cardiovascular disease and death that result from it [3].
Primary and secondary prevention of cardiovascular illnesses are greatly aided by lipid lowering therapy, which encompass both pharmacological and non-pharmacological approaches. Despite their widespread use and status as first-line pharmacological treatments, HMG Co-A reductase inhibitors are not without their drawbacks. Due to the fear of adverse events, patients often do not receive the recommended amount of treatment and do not accomplish their LDL goals. The feedback compensatory stimulation of the HMG Co A reductase enzyme causes statins to provide a ceiling dose effect with continuous use or even with increasing dosages [4, 5].
The practical use of successful pharmaceutical techniques for decreasing LDL has been associated with a decrease in cardiovascular events, according to studies. However, they are still only effective against a small subset of these endpoints. As a result, other parts of the lipid profile are attractive targets for reducing the disease load that remains. The outcomes of the trials for other newer treatments, such as PPAR-agonists, antisense oligonucleotides, and cholesteryl ester transfer protein inhibitors, have not been encouraging [6, 7].
New evidence of vitamin-mediated impacts on gene expression has emerged in recent years. Among these, biotin has demonstrated the ability to control the expression of genes critical

for intermediate metabolism. A B complex vitamin, biotin is currently utilised to treat dermatitis, brittle nails, hair loss, and the parental nutrition associated with biotin insufficiency. Pharmacological dosages of biotin reduce hypertriglyceridemia, according to studies that examined its effects in small patient groups. Research has also demonstrated that both diabetic and non-diabetic individuals can reduce their plasma lipoprotein levels by supplementing with biotin [8, 9].

The purpose of this research was to determine how dyslipidemia individuals' plasma lipid profiles were affected by therapeutic dosages of Biotin. Biotin has the potential to become an alternative to expensive and poorly tolerated lipid-lowering drugs for the treatment of dyslipidemia if its efficacy is demonstrated. In the long run, this will help lessen the impact of diseases [10, 11].

This study aims to compare the efficacy and adverse effect profile of biotin-atorvastatin combination therapy with that of atorvastatin monotherapy in order to ascertain the biotin-induced reduction of plasma lipids.

Methods

Following the acquisition of written informed consent, 50 patients with secondary dyslipidemia and ages 45 to 60 were included. This study was conducted at the Department of Pharmacology, Shree Lakshmi Narayana Institute of Medical Sciences Pudduchery, India between March 2019 to February 2020. They were randomly assigned to one of two groups after completing baseline laboratory examinations and lipid profiles. Those who served as controls. Received Atorvastatin 20 mg alone and the study group received Biotin 5mg combined with Atorvastatin 20 mg for 6 weeks. Twelve weeks of follow-up were conducted with both groups.

Inclusion Criteria

- Both sexes.
- 45-60 years old.
- Newly diagnosed instances of dyslipidemia with

Exclusion Criteria

- Individuals with very high plasma total cholesterol levels.
- Patients with uncontrolled Diabetes Mellitus.
- Ages under 45 and over 60.

Procedure

The Institutional Ethics Committee gave its clearance before the research could begin. At the Hypertension clinic, patients with Type 2 Diabetes mellitus or hypertension were informed about the study's goals and methods. Eighty patients were screened for this study based on their willingness to participate and provide written informed permission. The chosen patients were asked to sign an informed consent document in their native language.

Results

The selection criteria led to the exclusion of 20 patients; the remaining 50 were then divided into two groups of 30 patients each. No one in any of the groups decided not to continue. We calculated and tallied the mean ages, sex distributions, and baseline lipid profiles of both groups, as well as any related disorders such as diabetes mellitus and hypertension. Biotin was discontinued after 6 weeks of treatment, and for the subsequent 6 weeks, patients in the study group and those in the control group were administered Atorvastatin monotherapy in their respective departments. After 12 weeks, we checked the plasma lipid profiles and other laboratory measures of both groups again to see whether Biotin had any lingering effects. Throughout the 12-week research period, we diligently tracked any adverse occurrences and other impacts that were identified and recorded.

Table 1: Basic features of the two sets

Baseline Characteristics	Control Group (25) Mean	Study Group (25) Mean
Mean age in yrs.	49.50	49.86
Number of males	12	12
Number of females	13	13
Diabetes Mellitus	8	6
Hypertension	17	18
Baseline Lipids ((mg/dl))		
Total Cholesterol	262.88	285.88
LDL Cholesterol	159.12	172.55
Triglyceride	171.04	211.4
VLDL Cholesterol	35.44	42.00
10.HDL Cholesterol	45.32	46.14

The demographic and lipid profiles of the two groups are presented in Table 1. Both groups had a comparable incidence of diabetes mellitus. One fourteenth of the people in the study group's control group had diabetes mellitus. Both groups had comparable rates of hypertension. In the control group of the study, hypertension was found in 35 individuals.

Table 2: The two groups' mean ages

	Group	N	Mean	S. D.
Age (Yrs.)	Control	25	51.51	2.324
	Study	25	52.35	2.354

In Table 2, we can see that the two groups (Control and study) had similar average ages. In the study group, patients' mean age was 52.32 years, while in the control group it was 51.8 years. The average age of the two groups was not significantly different.

Table 3: Distribution of ages compared

Age interval	Control (25)		Test (25)	
	No	%	No	%
45-49 yrs.	10	36.66	9	40
50-54 yrs.	12	56.66	14	56.66
>55 yrs.	3	6.66	2	3.33
Total	25	100	25	100

Both the control and research groups' patient ages are displayed in Table 3. In contrast to the nine patients in the research group, ten in the control group were between the ages of 45 and 49. There were 26 people in the 50-54 age range in both the control and experimental groups. Two patients in the research group were in the 55-60 age bracket, whereas three in the control group were. The age distributions of the two groups were very similar. Patients in the 50–54 age group made up a larger proportion of the total.

Table 4: Distribution based on gender

	Group			
	Control		Study	
	Number	%	Number	%
Male	13	43.3%	13	43.3%
Female	17	56.7%	17	56.7%
Total	30	100	30	100

Discussion

Coronary heart disease, ischemic cerebrovascular disease, and peripheral vascular disease, all of which are caused by atherosclerosis, can be attributed, in part, to dyslipidemias. Medications that alter cholesterol levels have been the subject of ongoing study ever since hypercholesterolemia was recognized as a significant risk factor for cardiovascular disease and death. One of the most commonly prescribed medications, statins have been around since the late 1980s. Myalgia and other side symptoms, such as weakness, fatigability, and cognitive impairment, cause most patients to adhere to their statin treatment plans less than optimally in clinical practice. Patients who are unable to tolerate statins do not have many treatment choices [12-14].

Patients who are unable to take statins are being considered for clinical trials of other, less invasive lipid-lowering medications. Among these are more recent medications such as evolocumab, mipomersen, and lomitapide, which inhibit microsomal transfer protein and proprotein convertase subtilisin/kexin 9. Biotin is a vitamin that may be dissolved in water and functions as a substitute for carboxylases. On a genetic level, biotin controls intermediate metabolism as well. Biotin, according to mouse studies, lowers serum triglycerides and lipogenic gene expression when administered at pharmacological quantities. Based on these evidences and the fact that greater dosages of biotin do not have any harmful effects, it may be useful in managing hyperlipidemias [13, 15].

After 6 weeks of treatment, this scientific trial evaluated the efficacy and safety of taking 20 mg of Atorvastatin alone with taking 5 mg of Biotin every day. By removing patients less than 45 years of age at screening, the likelihood of inducing primary dyslipidemias is reduced, as these patients will exhibit symptoms at an early stage and have associated cardiovascular complications. Furthermore, a significant risk factor for atherosclerosis is age greater than 45 for men and 55 for women. Therefore, we have limited the trial to individuals who have recently been diagnosed with secondary dyslipidemias and are at high risk of atherosclerosis [14, 16].

Patients in the control group averaged 50.7 years of age, while those in the experimental group averaged 50.13. We have included male and female patients in the study, however the females outnumbered the males in both categories. There was no difference in the sex distribution between the two groups of patients. We found that all of the patients with hypertension in our study had moderately severe cases that were well treated. We enrolled individuals who were already diagnosed with type 2 diabetes mellitus; the study group had a diabetes mellitus incidence of 23.3%, whereas the control group had 26.6% [17, 19].

In terms of mean age, age distribution, sex distribution, and related co-morbid diseases, statistical analysis has shown that both groups are equivalent. Both groups had high rates of patient compliance, with 100% of patients attending their scheduled appointments. All patients in the trial group were able to finish the programme, and the follow-up was excellent. Although there was no statistically significant difference between the groups at the end of the first week, the combination therapy group had a 16.06% reduction in total cholesterol and the monotherapy group had a 16.7% reduction; this suggests that biotin did not have any early effects on the study population [18, 20].

Afterwards, total cholesterol decreased by 26.32% at the end of the second week, 28.33% at the end of the fourth week, and 28.68% at the end of the sixth week as a result of monotherapy. Total cholesterol in the combination therapy group decreased by 34.66% at the end of the second week, 41.33% at the end of the fourth week, and 40.37% at the end of the sixth week, in that order. From the second week forward, there was a larger reduction in total cholesterol with the combination of biotin 5 mg and atorvastatin 20 mg. This difference was statistically significant and was well-maintained until the sixth week. Biotin does not appear to have any lingering effects on plasma lipoproteins, since the percentage reduction in the study group was 29.96% at the follow-up visit, comparable to the 27.56% reduction in the control group [21, 23].

In the control group, LDL levels dropped by 19.08% in the first week, 34.35% in the second week, 35.69% in the fourth week, and 36.09% in the sixth week, respectively. Previous research has shown a 25-40% reduction after 12 weeks of treatment with 20 mg of Atorvastatin, thus these reduction rates are comparable. In the first week, the study group's LDL levels dropped by 16.90%; in the second week, they dropped by 39.89%; in the fourth week, they dropped by 42.62%; and in the sixth week, they dropped by 43.28%. At the 2nd, 4th, and 6th weeks, statistical analysis showed a statistically significant difference in the percentage reduction of LDL levels between the study group and the control group. There was no evidence of delayed biotin effects on LDL levels at the follow-up visit, since both groups showed comparable reduction percentages [22, 24].

As early as the first week of treatment, the triglyceride levels began to drop considerably due to the combo medication. In comparison to the control group, which showed a 5.66% reduction at the end of the first week, an 18.34% reduction at the end of the second week, a 19.88% reduction at the end of the fourth week, and a 20.66% reduction at the end of the sixth week, the study group achieved a range of mean triglyceride reductions: 13.96% at the end of the first week, 25.92% at the end of the second week, 25.65 at the end of the fourth week, and 28.45% at the end of the sixth week. From week one through week six, there was a statistically significant difference in the reduction percentages [23, 25].

Combination therapy with biotin and atorvastatin resulted in a greater decrease of total cholesterol, LDL, and triglyceride levels compared to monotherapy with atorvastatin, according to this study. The genes involved in glucose and lipid hemostasis maintenance and intermediate metabolism

are regulated by biotin, which is why it lowers lipids. As a result, biotin can be a safe and effective supplemental medication for atorvastatin. Further trials in dyslipidemias should explore biotin treatment alone as a potentially useful therapy for patients with dyslipidemia to avoid coronary artery disease and cerebrovascular damage [24, 25].

Conclusion

Results show that compared to Atorvastatin 20 mg alone, a combination therapy including 5 mg of biotin and 20 mg of atorvastatin reduces total cholesterol, LDL cholesterol, and triglycerides more effectively with fewer side effects. Adjuvant hypolipidemic therapy with biotin is thus a safe and well-tolerated option for treating secondary dyslipidemias.

Funding

None.

Conflict of Interest

None.

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