AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Study on Prevalence and Management of Risk Factors Associated with Secondary Dyslipidemia

S. Sriram*[1], N. Senthivel[2], Elda Maria Dominic[1], Murali Krishna Kandukuri[1], Anju Aleyamma Sabu[1]

1. Department of Pharmacy Practice, College of Pharmacy, SRIPMS, Coimbatore,TN, India.
2. Senior Consultant, Department of General Medicine, Sri Ramakrishna Hospital, Coimbatore.

ABSTRACT

To assess the prevalence and types of lipid abnormalities, analyze the rationalein the drug therapy and drug interactions in the drug therapy. Each patient's medication profile was reviewed and patients who met the inclusion criteria were briefed on the study. The data from medical charts of all the cases with lipid abnormality were recorded during ward rounds. The study population included patients with primary dyslipidemia (38.8%) and secondary dyslipidemia (61.2%). The major concomitant disease was systemic hypertension followed by Diabetes Mellitus. Majority of the patients were in non CHD category. 88.7% of non CHD patients had 2+ risk factors and 11.3% had 1 risk factor. The non CHD group were subjected for estimation of 10 year risk percentage for having CHD using Framingham's scale in which 92% of non CHD patients had ≤ 20% ten year risks for having CHD. The drug interactions with lipid lowering agents were 33.3% and without lipid lowering agents were 66.7%. The major drug interactions with lipid lowering agents were high. Conclusion: Results revealed that Diabetes, Thyroid Disorders, Nephrotic Disorders are responsible for elevation of lipid profiles. Some dyslipidemias appear to be refractory to drug treatment in the presence of an ongoing unrecognized secondary cause.

Keywords: Dyslipidemia, CHD, Diabetes Mellitus, Framingham's scale, lipid lowering agent, Thyroid, Nephrotic.

INTRODUCTION

The major lipids in the body are cholesterol, triglycerides and phospholipids. They are transported as complexes of lipid and proteins known as lipoproteins. The three major classes of lipoproteins in serum are low-density lipoproteins (LDLs), high-density lipoproteins (HDLs), and very-low-density lipoproteins (VLDLs)[1]. Dyslipidemias are lipoprotein metabolism disorders, which includes lipoprotein overproduction or deficiency. These disorders are manifested by elevation of the serum total cholesterol, LDL cholesterol and triglyceride concentrations, and a decrease in the high-density lipoprotein (HDL) cholesterol concentration[2]. Atherogenic dyslipidemia is a combination of elevated triglycerides, small-dense LDL particles, and low levels of HDL-cholesterol[3]. High cholesterol leads to increase risk of heart disease, heart attack, and stroke. When too much cholesterol circulates in the blood, it creates sticky deposits, called as plaque, along the artery walls. Plaque eventually narrow down or block the flow of blood to the brain, heart and other organs. Some blood cells that gets caught on the plaque form clots, which may break loose to completely block blood flow through an artery, causing heart attack or stroke[4]. Secondary causes are the most common causes of dyslipidemia in adults. Another most important secondary cause in developed countries is a sedentary lifestyle with excessive dietary intake of saturated fat, trans fats and cholesterol. Other common secondary causes include diabetes mellitus, chronic kidney disease, alcohol overuse, hypothyroidism, primary biliary cirrhosis and other cholestatic liver diseases, and drugs, such as thiazides, retinoids, β-blockers, estrogen and progestins, highly active antiretroviral agents and glucocorticoids[5].

Complications of Dyslipidemia

Dyslipidemia is a major risk factor for atherosclerosis. Atherosclerosis is a disease process that effects the coronary, cerebral and peripheral arterial circulation.

A.   Stroke

Stroke is a term that describes a clinical event caused either by occlusion or hemorrhage in the arterial supply to the central nervous system resulting in tissue infarction. Atheroma formation is the root of pathogenesis of thromboembolic stroke. Observational studies suggest that dyslipidemia particularly high LDL-C, low HDL-C and high triglyceride are important risk factors for thromboembolic stroke.

B.   Peripheral artery disease (PAD)

It is most commonly a manifestation of systemic atherosclerosis in which the arterial lumen of the lower extremities becomes progressively occluded by atherosclerotic plaques. There is a growing evidence that atherosclerosis in the peripheral circulation should be considered in the same manner

as atherosclerosis in the coronary circulation. Patients with PAD, even in the absence of history of myocardial infarction or stroke, have approximately the same relative risk of death from cardiovascular causes as do patients with a history of coronary or cerebrovascular disease.

C.   Coronary Heart Disease

The etiology of atherosclerosis is a multifactorial but the cost effective relationship between dyslipidemia and atherosclerosis has been shown in many studies and trials.It has been shown that reducing the plasma LDL- C levels sharply reduces the risk of subsequent clinical CHD in both patients with pre-existing CHD and in patients free of CHD. Evidence suggest that oxidative modification of LDL within the artery is necessary for mediating its atherogenicity[6].

DISEASE STATES

1. **Diabetes mellitus:** Cardiovascular disease is the major cause of death in persons with type 1 diabetes. Insulin resistance plays an important role in the development of Dyslipidemia [7].
    - Type 1- Increase triglycerides, LDL and HDL C may be high or normal[8].
    - Type 2- Increase triglycerides, LDL, Apo-B and decrease HDL C[9, 10].

2. **Hypothyroidism:** TC, LDL-C, VLDL-C and TG levels were elevated in patients with overt hypothyroidism.Subclinical Hypothyroidism is associated with increased levels of TC and LDL-C. Moreover, some studies have shown that Subclinical hypothyroidism and dyslipidemia may also be accompanied by increased TGs and decreased HDL-C levels[11].

3. **Chronic Renal Failure:** Chronic Renal Insufficiency causes an increase in VLDL and triglyceride concentrations and lowers HDL cholesterol concentrations. Total cholesterol and LDL-cholesterol concentrations may be normal or even slightly lower than those in the general population[12].

4. **Nephrotic Syndrome:** Increase in the plasma levels of cholesterol, LDL, triglycerides and lipoprotein (a) often occur. Total HDL-cholesterol levels are usually normal or reduced in the nephrotic syndrome[13].

5. **Obesity:** Overweight and obesity are associated with hyperlipidemia. Obesity causes hypertriglyceridemia, a high level of LDL and a low level of HDL cholesterol[14].

6. **Alcoholism:**Alcohol has an additive effect on the postprandial triglyceride peak when it is accompanied by a meal containing fat, especially saturated fat. This results in a decrease in the breakdown of chylomicrons and VLDL remnants due to an acute inhibitory effect of alcohol on lipoprotein lipase activity. Moreover, alcohol increases the synthesis of large VLDL particles in the liver, which is the main source of triglycerides that leads to hypertriglyceridemia[15].

7. Due to certain drugs

   a) Antihypertensive agents

      i.   Diuretics: Hydrochlorothiazide increases TCH and LDL- C [16].Thiazide treatment of hypertension increases LDL-C, triglycerides and the LDL / HDL ratio [17].

      ii. Beta blockers: Increase serum triglyceride, decrease HDL-CH with no effect on LDL [16].

   b) Oral contraceptives

Increases in plasma triglyceride levels were observed in normal young women treated for two weeks with an oral contraceptive containing ethinyl estradiol and medroxyprogesterone [18].

   c) Corticosteroids- Prednisolone

Glucocorticoids elevate triglycerides and raise levels of HDL-C. Anabolic steroids when taken orally reduce levels of HDL- C in contrast to injectable testosterone, which does not adversely affect the LDL-to-HDL ratio[19].

Keeping this in view, present study was undertaken to assess the prevalence and types of lipid abnormalities, analyze the rationale and drug interactions in the drug therapy.

MATERIALS AND METHODS

A prospective study was carried out for six months by the Department of Pharmacy Practice in a 700 bedded multi-specialty hospital located at Coimbatore. The department selected for the study was the department of General Medicine. A pilot study for a period of fifteen days was carried out to know the scope of the study in the department of General Medicine. Knowledge on the patient perception, and risk factors associated with dyslipidemia will help the health care professionals to ensure the better treatment outcomes. The study was approved by the Dean of the hospital. The study protocol was submitted to the institutional ethics committee and the same was approved by the committee. The study was conducted with the expert guidance of senior and junior physicians of the study department. The author was permitted to utilize the hospital facilities to make a follow up of the cases, in the selected departments. All the health care professionals were well informed through Dean's official circular. A total number of 85 patients who met the inclusion criteria were enrolled in the study.

RESULTS AND DISCUSSIONS

85 patients who met the inclusion criteria were enrolled in the study. The study population included 38.8% with primary dyslipidemia and 61.2% with secondary dyslipidemia [Table 1]. The

major concomitant disease in the study population was systemic hypertension which was seen in 45.9% of the patients followed by Diabetes Mellitus which was seen in 35.3% [Table 2]. There were 27% patients in CHD category and 72.9 % were in non CHD category [Table 3]. The results shows 88.7% of non CHD patients in study population had 2+ risk factors and 11.3% patients was with 1 risk factor [Table 4]. The patients in non CHD group were also subjected for estimation of 10 year risk percentage for having CHD using Framingham's scale. The results revealed that in 92% study population, non CHD patients were having ≤ 20% ten year risks for having CHD [Table 5]. During the study it was found that the study population had a mean scores of LDL-C 151.4, total cholesterol 218, HDL-C 43.2, VLDL –C 23.8 and TRG 127.3 [Table 6]. The results revealed that the drug interactions with lipid lowering agents were 33.3% and drug interactions without lipid lowering agents were 66.7% [Table 7]. The drug interactions with lipid lowering agents revealed that major interactions were high with 57.3% followed by moderate 42.7%. In the present study, the results on the major drug interactions observed, indicated that the HMG- CoA reductase inhibitor- Atorvastatin, had frequent "major" drug interactions.

Table 1: Types of Dyslipidemia

Types	No. of Population	Percentage (%)
Primary	33	38.8
Secondary	52	61.2

Table 2: Co-Morbidities Among Study Population

CO-Morbidities	Total number	Percentage (%)
DM	30	35.3
SHT	39	45.9
HYPOTHYROIDISM	08	9.4
CRF	02	2.3
CHD	23	27.1

Table 3: Categorization of CHD Groups

Category	Total number	Percentage (%)
CHD Group	23	27.1
Non CHD Group	62	72.9

Table 4: Number of Risk Factors Among Non CHD Patients

Risk factors	Total number	Percentage (%)
0-1	07	11.3
2+	55	88.7

Table 5: Estimation Of 10-Year Risk %for Having CHD

10 Year risk %	Total number	Percentage (%)
≤ 20	57	92
>20	05	08

Table 6: Average Lipid Profile

Profile	Average Value
LDL-C	151.4
Total-C	218
HDL-C	43.2
TRG	127.3
VLDL-C	23.8

Table 7: Number of Drug Interactions with Lipid Lowering Agents

Agents	Drug interactions	Percentage (%)
With Lipid lowering agents	75	33.3
Without lipid lowering agents	150	66.7

CONCLUSION

It was found that secondary dyslipidemia were more in the study setup than the primary dyslipidemia. Current guidelines for hyperlipidemia state that clinicians should evaluate for underlying conditions that could be causing or exacerbating dyslipidemias before initiating or intensifying the treatment in their patients. In our study Diabetes Mellitus was found to be one of the major cause of secondary dyslipidemia. These conditions referred to as "*secondary causes*" of dyslipidemia are important to identify for several reasons. Some associated diseases are important health issues to recognize (E.g., chronic kidney disease, DM) and the dyslipidemia may be one of the first clues to the diagnosis. Although several lipid-altering therapies have been shown to benefit patients who are at risk for CHD, lowering of LDL- C with HMG CoA reductase inhibitors (statins) has shown the most striking results. Literatures revealed that combining statins with fibrates or niacin offers significant reductions in TG and increases in HDL. Recognizing the drug interactions and co-morbidity may alter subsequent treatment decisions (e.g., identifying potential drug interactions, diagnosing hypothyroidism, which may increase the risk for statin-related myopathy). But literatures documented that some dyslipidemias can appear to be refractory to drug treatment in the presence of an ongoing unrecognized secondary cause. For example, untreated DM or excessive alcohol intake can render medical therapy of hypertriglyceridemia much less effective. Although numerous factors have been linked to adverse lipoprotein changes, their prevalence and clinical importance remain poorly described. Working collaboratively with patients, physicians, and other health care providers, pharmacists who have ready access to

objective clinical data and the necessary knowledge, skills and resources can provide an advanced level of care that results in successful management of dyslipidemia. Clinical Pharmacists should take-up such studies for effective patient care.

ACKNOWLEDGEMENT

REFERENCES

1.   Dipiro J.T, Talbert R.L, Yee G.C, Matzke G.R, et al. Pharmacotherapy: A Pathophysiologic Approach. 7th Edition, USA: McGraw- Hill; 2008, 385-404.

2.   Ahmed S.M, Clasen M.E, Donnelly J.F. Management of Dyslipidemia in   Adults. American Family Physician. 1998 May, 57(9):2192-2204.

3.   Misra A., Luthra K., Vikram N.K. Dyslipidemia in Asian Indians: Determinants and Significance. Journal of The Association of Physicians of India. 2004 Feb; 52: 137-142.

4.   Hypercholesterolemia, University of Maryland Medical Center. Available from:http://umm.edu/health/medical-reference-guide/complementary-and-alternative-medicine-guide/condition/hypercholesterolemia

5.   Dyslipidemia, The Merck Manual, September 2013. Available from: http://www.merckmanuals.com/professional/endocrine_and_metabolic_disorders/lipid_disorders/dyslipidemia.html?qt=dyslipidemia&alt=sh

6.   Tripathi K.D. Essentials of Medical Pharmacology. 6th ed,Jaypee Brothers medical publishers LTD; 612-621.

7.   Vergès B. Lipid Disorders in Type 1 Diabetes. Type 1 Diabetes - Complications, Pathogenesis, and Alternative Treatments. InTech. 2011; 45-60.

8.   Groop P.H, Thomas M.C, Mills V. et al. HDL Composition Predicts New-Onset Cardiovascular Disease in Patients with Type 1 Diabetes. Diabetes care. 2007 Oct, 20: 2706-2707.

9.   Dyslipidemia in Adults with Diabetes. Canadian Diabetes Association, Clinical Practice Guidelines Expert Committee.Canadian Journal Of Diabetes. 2006, 30(3):230-240.

10. Tkac I. Treatment of dyslipidemia in patients with type 2 diabetes; Overview and meta-analysis of randomized trials. Science Direct. 2007 Nov; s23- s28.

11. Rizos CV, Elisaf MS, Liberopoulos EN. Effects of Thyroid Dysfunction on Lipid Profile. The

Open Cardiovascular Medicine Journal.2011 Jan; 5: 76-84.

12. Mesquita J, Varela A, Medina JL. Dyslipidemia in renal disease; Causes, consequences and treatment. Endocrinología Y Nutrición. 2010 Jun; 57(9): 440–448.

13. Radhakrishnan J., Appel G.B. Lipid abnormalities in nephrotic syndrome. UpToDate. 2013 Jul; obtained from www.uptodate.com

14. Lai SH, Nga KC, Lin HF, Chen HL. Association between Obesity and Hyperlipidemia among Children. Yale Journal of Biology and Medicine. 2001; 205-210.

15. Van de Wiel A. The effect of Alcohol on postprandial and fasting triglycerides. International Journal of Vascular Medicine. 2011 Aug; Volume 2012, Article ID 862504.

16. M Middeke, W O Richter, P Schwandt, B Beck and H Holzgreve therapy with beta blockers and diuretics. Normalization of lipid metabolism after withdrawal from antihypertensive long-term. The Journal of American Heart Association. 1990.

17. Stable E.P, Caralis P.V. Thiazide-induced disturbances in carbohydrate, lipid, and potassium metabolism. American Heart Journal**.** 1983 Jul; 106(1)-2: 245–251.

18. Hazzard W.R., Spiger M.J, Bagdade J. D., BiermanE.L.Studies on the Mechanism of Increased Plasma Triglyceride Levels Induced by Oral Contraceptives.New England Journal of Medicine. 1969 Feb; 280: 471-474.

19. Stone N.J. Secondary causes of Dyslipidemia. Med Clin North Am.1994 Jan; 78(1): 117-141.