ORIGINAL ARTICLE

PROSPECTIVE, PHARMACOEPIDEMIOLOGIC STUDY OF PRESCRIBING PATTERNS FOR LIPID LOWERING DRUGS AT A TERTIARY CARE TEACHING HOSPITAL IN EAST INDIA

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ABSTRACT

Background: The guidelines for management of dyslipidemia released by the US National Cholesterol Education Program (NCEP) have been in use throughout the world. But South Asian Indian populations are reported to have significantly different lipoprotein parameters and atherogenic risk factors than Western populations. Even now there is paucity of data regarding the drug use pattern of the lipid lowering drugs in India.

Objective: The aim of this study was to determine current prescribing patterns for lipid-lowering drugs (LLDs) adopted by physicians in East India.

Methods: This prospective, non-interventional, uncontrolled, open-chart, pharmaco-epidemiologic study was conducted from June 2010 to May 2011 at a tertiary rare hospital in East India and included 200 dyslipidemic patients. The pattern of prescribing LLDs was recorded, along with the serum levels of lipid parameters – total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) – at the time of initiating LLD therapy.

Results: Males above 40 years were predominantly prescribed (89.5%) lipid lowering (LLDs) drugs. Advice regarding life style modification was included in only 18% of prescriptions. The ratio of prescribing LLDs for primary and secondary prevention of coronary artery disease was 1:1.15. The LLDs prescribed were statins (80.5%) and fibrates (14.5%). The mean (SD) values of lipid parameters in the study population showed high total cholesterol, LDL-C, borderline high triglyceride as per the NCEP guidelines as follows: total cholesterol (TC): 233.54±21.5, LDL cholesterol (LDL-C): 149.65±25.6, triglycerides (TG): 216.062±34.5 and HDL cholesterol (HDL-C): 39.904±5.5.

Conclusions: The prescribing patterns of the lipid lowering drugs (LLDs) was in accordance with the specific recommendations made for the South Asian Indian populations, as well as with the 2001 NCEP – III guidelines.

Keywords: Dyslipidemia, prescribing pattern, low density lipoprotein – cholesterol, total cholesterol, high density lipoprotein – cholesterol, triglycerides.

INTRODUCTION

Coronary heart disease (CHD) is the leading cause of death in the industrialized world[1] with the global burden of disease continuing to increase[2]. The Indians with CHD have a distinctive lipid profile, characterized by low level of high-density lipoprotein cholesterol (HDL-C), high level of triglycerides (TG) and increased lipoprotein (a) [lp(a)] [3].

Dyslipidemia has gained importance among various factors implicated in the cause of atherosclerosis[4]. Each component of the lipid profile (i.e., high serum levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG), and low serum levels of high-density lipoprotein cholesterol (HDL-C) contributes uniquely to atherogenesis[5, 6, 7]. The role of active management of dyslipidemia and the benefits of using lipid-lowering drugs (LLDs) to bring the lipid profile to the desired range have been well established [8, 9], but how these drugs are prescribed or used in the general population has not been studied extensively in the eastern India. Most of the studies are among western population[10, 11, 12] and some from other parts of India [13]. Thus, a study of prescribing patterns is needed from Eastern India. Prescribing pattern studies are of special importance in conditions where there are

no universal guidelines, especially if the drugs under consideration are potentially toxic or likely to be used for prolonged periods.

The US National Cholesterol Education Program (NCEP) issued guidelines for the management of dyslipidemia in 1988, 1993, and 2001. These guidelines were based on evidence accumulated in the study of cholesterol management. However, most trials used in the development of these guidelines looked at the role of various lipid fractions in coronary artery disease (CAD) in Western countries and induced mostly white patients[12, 14, 15]. There has been some controversy over the relevance and applicability of these guidelines to the treatment of dyslipidemia in South Asian Indian populations including residents of India, Pakistan, Bangladesh, Sri Lanka, Nepal, Bhutan and Afghanistan.

In India, there has been a paradoxical increase in incidence of CAD in recent years[16]. This has been attributed to the prevalence of high serum TG levels and low HDL-C levels. A high prevalence of diabetes mellitus and the so-called emerging risk factors – including raised serum levels of lipoprotein (a) [Lp(a)], homocysteine, fibrinogen, plasminogen activator inhibitor, apolipoprotein B, and C-reactive protein, and low serum levels of apolipoprotein A – I – also have been implicated in this paradox.

These major differences in the prevalence of dyslipidemia and risk factors in South Asian Indian indicate that this subpopulation requires a treatment strategy different from that suggested for the Western population. The revised NCEP guidelines issued in 2001 is in accordance to Indian population.

With this background, the present study was conducted to assess current prescribing patterns for lipid-lowering drugs (LLDs) adopted by physicians in East India.

MATERIAL AND METHODS

Study site and population: The present study was conducted among the out patients attending the Department of Medicine and Department of Cardiology, SCB Medical College and Hospital, Cuttack. Cuttack is a city in the state Odisha in Eastern India. The hospital is situated in the heart of the city and a large proportion of patients from not only Cuttack but also from other parts of Odisha as well as from neighbour state West Bengal attend this hospital.

Study design and Sample size: This was a prospective, non-interventional, uncontrolled, open-chart, pharmaco-epidemiologic study. Data was collected from 200 outpatients attending the Department of Medicine and Department of Cardiology.

Study tools, inclusion criteria and study parameters: Data was collected using a pre-designed, pre-tested proforma. Data regarding demographic profile of patients like age, sex and the prescribing pattern of lipid lowering drugs (LLDs) were collected from 200 prescriptions after a pilot study of 30 prescriptions, which were independently analyzed by various prescribers at SCB Medical College.

The inclusion criteria were as follows: any age; either sex; prescribed LLDs for the first time; baseline levels of various serum lipoprotein parameters (serum TG, TC, HDL-C, LDL-C) estimated in the central laboratory of the hospital.

The first 200 patients satisfying these criteria were enrolled during visits to the Medicine and Cardiology outpatient department during June 2010 to May 2011. The demographic profile of patients and prescribing pattern of LLDs were recorded on the standardized proforma. The prescribers were unaware of the study and its objectives.

Statistical analysis:

After collection of data it was double entered in Microsoft Excel sheet and verified. A clean database was generated and entered in SPSS version 16.0. After this the data was analyzed in SPSS version 16.0. Proportions of patients using different lipid lowering drugs were calculated. Percentage of patients receiving different advices of life style modification like verbal, prescription and combination of both were analyzed. Mean and standard deviation of different lipoprotein parameters were calculated for comparison.

RESULTS

The demographic profile of the patient showed that of the 200 patients who received LLDs, 89.5% were above 40 years of age (179/200) and 10.5% were between 18 – 39 years (21/200). Among the study population 72% were males (144/200) and 28% were females (56/200).

Table 1: Demographic Profile of Patients (n=200)

Parameters	Patients (%)
Age	
18 – 39 Yrs	21 (10.5)
40 – 75 Yrs	179 (89.5)
Sex	
Male	144 (72.0)
Female	56 (28.0)

In addition to receiving an LLD, instructions regarding therapeutic lifestyle (in terms of dietary modification and regular physical exercise) were given to 94% overall (188/200) 18% on prescription (36/200), 89% verbally (178/200), 13% both on prescription and verbally (26/200). The number of patients prescribed LLDs for primary and secondary prevention of coronary artery disease were 93 (46.5%) and 107 (53.5%); so the ratio was 1:1.15.

Analysis was done to assess the advice given for life style modification according to age of the patient. It was found that among patients aged less than 40 years

of age, all were given some advice for life style modification: either verbal or on prescription or both. But 12 (6.7%) of the older patients were not given any advice for life style modification. 57% of the younger patients in contrast to 78% of the older patients were advised only verbally for life style modification. These differences were found to be statistically significant (p=0.012).

Life style modification advice was also analyzed according to the sex of the patients. It revealed that 2% of male patients were not given any advice for life style modification. On the other hand 14% female patients were not given any advice. This difference was again proved to be statistically significant (p=0.013).

Table 2: Advice Given to the Patients (n=200)

Advice	Patients (%)
Life style Modification (n=188)	
Prescription	36 (18.0)
Verbally	178 (89.0)
Both	26 (13.0)
Drugs prescribed for primary prevention of CAD	93 (46.5)
Drugs prescription for secondary presentation of CAD	107 (53.5)

Table 3: Life Style Modification Advice According to the Age of the Patients (n=200)

Parameters	Life style modification advice				Total (%)	χ^2 (df), P value
	Verbal (%)	Prescription (%)	Verbal + Prescription (%)	Nil (%)		
Age (yrs)						
18-39	12 (57.1)	2 (9.5)	7 (33.3)	0 (0)	21 (100)	10.93 (3), 0.012
40-75	140 (78.2)	8 (4.5)	19 (10.6)	12 (6.7)	179 (100)	
Sex						
Male	110 (76.9)	7 (4.9)	22 (15.4)	4 (2.8)	143 (100)	10.84 (3), 0.013
Female	42 (73.7)	3 (5.3)	4 (7.0)	8 (14.0)	57 (100)	

Table 4: Details of Lipid Lowering Drugs Prescribed (n=200)

LLD Prescribed	Dose (mg/day)	Patients (%)
Statins		161 (80.5)
Atorvastatin	20	147 (73.5)
Simvastatin	20	8 (4)
Rosuvastatin	10	6 (3)
Fibrates		
Fenofibrate	200	29 (14.5)
Combined		
Atorvastatin + Ezetimibe	20+10	10 (5)

Of the lipid lowering drugs (LLDs) prescribed, 80.5% (161/200) of patients were prescribed the statins and 14.5% (29/200) were prescribed the fibric acid derivatives (fibrates) 5% (10/200) were prescribed a combination of Atorvastatin and Ezetimibe. Among the statins, Atorvastatin 73.5% (147/200) was commonly prescribed.

The mean ± SD levels of lipid parameters in the study population were as follows: TC, 233.54 ± 21.5 mg/dl; LDL-C, 149.65 ± 25.6mg/dl; TG, 216.062 ± 34.5, HDL-C, 39.9 ± 5.5 mg/dl

Table 5: Baseline Mean ± SD Values of Serum Lipoprotein Parameters

	TC (mg/dl))	LDL-C (mg/dl)	TG (mg/dl)	HDL-C(mg/dl)
Patients prescribed Statins (n= 161)				
Atorvastatin (n= 147)	224.68±21.25	144.51±19.14	190.66±35.19	41.09±5.15
Simvastatin (n=8)	228.88±7.55	145.95±8.39	213.42±6.80	40.1±1.54
Rosuvastatin (n=6)	244±42.54	164.46±49.76	184.33±33.69	39.33±5.98
Patients prescribed Fibrates (n=29)				
Fenofibrate	213.46±9.64	114.64±12.33	319.7±43.26	35.7±2.27
Patients prescribed Combined therapy (n=10)				
Atorvastatin + Ezetimibe	256.7±22.75	178.7±24.69	172.2±27.21	43.3±5.07

DISCUSSION

The threshold lipoprotein levels at which LLD therapy were started was lower than those indicated in the NCEP-II guidelines. The NCEP-II threshold values for initiation of drug therapy are based only on LDL-C values, recommending drug therapy for patients with LDL-C > 190mg/dl in the absence of coronary heart disease (CHD) and > 130 in the presence of CHD.

The ratio of prescribing LLDs for primary and secondary prevention of CAD has been suggested as the best indicator for identifying quality of prescribing, because efficient management of dyslipidemia can prevent morbidity and mortality due to atherosclerosis. In the present study, this ratio was 1:1.15 (46.5% vs. 53.5%), which shows a good quality of prescribing because 46.5% of dyslipidemic patients received LLDs for prevention of atherosclerotic complication. Advice regarding therapeutic lifestyle changes, in the form of dietary modification and regular exercise, was included in only a small number of prescriptions (18%). Maximum numbers of patients were advised verbally

(89%). There is considerable room for improvement in this prescribing practice because it has been well documented that a 10% to 20% decrease in TC levels and a 5% to 20% decrease in LDL-C levels can be achieved with lifestyle changes alone with proper patient education.

The prescribing pattern of LLDs shows that of the various LLDs available drugs from only 2 groups were mainly prescribed: statins (80.5%), fibrates (14.5%). This finding is in accordance with prescribing trends in western populations, in which statins are the most commonly prescribed LLD. Other LLDs i.e. combination of Atorvastatin and Ezetimibe 15%) has been advised in small number of patients. Ezetimibe is the first in a novel class of selective cholesterol absorption inhibitors. It has synergetic effect with statins and offers a new approach in reaching therapeutic goals.

As per the NCEP criteria for classification of lipoprotein values, the mean ± SD values of all the patients showed that overall the study population had high total cholesterol, LDL-Cholesterol, borderline high triglyceride. This dyslipidemic picture is different from that in the North where high triglyceride stands out as major risk factor.

Another important consideration is that statins do not lower raised Lp(a) levels. In fact both Simvastatin and Atorvastatin can significantly raise serum Lp(a) levels in patients whose levels are already increased. In contrast, a fibric acid derivative is beneficial in lowering raised serum Lp(a) levels.

The NCEP-II guidelines were released in May 2001 with some major revision, including the following : considering diabetes mellitus as a CAD risk equivalent, decreasing desirable levels of LDL-C and TG to < 100mg/dl and < 150mg/dl respectively, initiating LLDs for patients with TG > 300mg/dl, raising HDL-C target values to > 40mg/dl, and recognizing Lp(a) levels > 30mg/dl as a significant emerging risk factor for the development and progression of atherosclerosis.

NCEP recommends initiation of LLD therapy with statins, most of the patients in the present study were also prescribed statins.

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