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Prescription pattern analysis of lipid lowering drugs in diabetic dyslipidaemia population in a tertiary care teaching hospital in Kerala

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ABSTRACT

Cardiovascular disease is the major cause of mortality and morbidity in patients with type2 diabetes mellitus. The US National Cholesterol Education Program (NCEP) has released guidelines for the management of dyslipidaemia which is currently followed worldwide. Since the Indian populations are reported to have significantly increasing CHD risk, it is a necessity to analyse the pattern of Lipid Lowering Drugs (LLDs) in diabetic dyslipidemic population to provide better patient care. The aim of this study was to analyse current prescribing patterns for lipid-lowering drugs (LLDs) in type 2 diabetic population in a tertiary care teaching hospital in Kerala. This prospective observational study was conducted from January 2016 to June 2016 at a tertiary care teaching hospital in Kerala and included 165 diabetic dyslipidemic patients. The pattern of prescribing LLDs was analysed, 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) before initiating the hypolipidemic therapy. The results of our study shows that statins were the most prescribed hypolipidemic agent (100%), out of which 96.36% were prescribed with atorvastatin and 3.63% with rosuvastatin. 33.33% of atorvastatin was prescribed in an age group of 60-69 yrs. The majority of rosuvastatin was prescribed in the same age group and it was found to be as 1.81%.The prescribing patterns of the lipid lowering drugs (LLDs) were in accordance with the current NCEP ATP III Guidelines.

INTRODUCTION

Lipoprotein metabolism disorder is most common in Type 2 Diabetes Mellitus and is known as Diabetic Dyslipidemia. It is characterized by increased total cholesterol, increased triglycerides (TG), increased low density lipoprotein cholesterol (LDL-C) and decreased high density lipoprotein cholesterol (HDL-C) [1].Cardiovascular disase (CVD) is a primary cause of morbidity and mortality among patients with hyperglycemia or type 2 diabetes mellitus (DM). It is estimated that between 60% and 80% of persons with diabetes will develop cardiovascular disease [2]. The aim of this study was to analyse the prescription pattern of hypolipidemic agents in diabetic population with cardiovascular disease. The most common lipid pattern in patients with DM includes hypertriglyceridemia, increased concentrations of small dense low-density lipoprotein particles, low levels of high density lipoprotein cholesterol (HDL-C), increased remnant lipoproteins, and elevated apo lipoprotein B concentrations. Multiple guidelines writing groups advocate combination therapy for the management of multiple lipid abnormalities (NCEP ATP III, ADA, and AHA/ACC) [2]. The aim of this panel was to develop guideline for detection, evaluation and treatment of high blood cholesterol in adults. NCEP ATP has been the revising and framing guideline which help the physician to provide better

treatment to cardiovascular patients. It also aims at educating the general population. All three guidelines ATP I, ATP II and ATP III have targeted low density lipoprotein as their primary goal.

ATP I is a high cholesterol management guideline in adult aged more than 20 years, published in the year 1988. It has been developed as a strategy for primary prevention of CHD in individual with high LDL-C >160mg/dl or with borderline high LDL-C 130-159mg/dl including more than two risk factors. ATP I guideline stressed on dietary therapy.

ATP II released in 1993, aims at primary prevention of CHD with LDL goal <160mg/dl for those with<2 CHD risk factors and target LDL-C<130mh/dl for those with ≥2 risk factors. This guideline also recognized HDL cholesterol <35mg/dl as risk factor and >40mg/dl as protector of CHD risk. ATP II stressed more on non-pharmacological therapy mostly in males aged less than 35 years including premenopausal women. Hypolipidemic agents were indicated for those patients with LDL-C >220mg/dl or with multiple CHD risk factor. For TG lowering no specific goals were specified by ATPII. ATP II recommended treatment with bile acid sequesterants or statins in combination with fibric acid for diabetic dyslipidemia.

In 2001, ATP III was published. The full report was published in December 2002. In our study NCEP ATP III, which is currently followed worldwide is used for the evaluation of data. It provides evidence-based recommendations on the management of high blood cholesterol and related disorders. The guideline provides recommendation for the management of high blood cholesterol and related abnormalities and by maintaining continuity with previous two guidelines. ATP III also introduced the concept of risk and risk assessment as the first step in risk management strategies. For high risk patients with high TG or low HDL-C a fibrate or nicotinic acid is combined with LDL lowering agent. If LDL ≥100mg/dl in high risk patients recommendations were given for LDL-C lowering drugs along with therapeutic life style changes [3, 4, 5].

Lipid lowering drugs such as statins lower LDL-C cholesterol and non-HDL-C and fibrates modestly raises HDL-C. They have an adjunctive role in the treatment of patients with high triglycerides/low HDL, especially in combination with statins. Nicotinic acid is another class of drug that elevates HDL-C. Several trials show the efficacy of nicotinic acid in reducing CHD risk, both when used alone and in combination with statins. This combination therapy produces a marked reduction of LDL-C and as well as an increase in HDL-C [5]. Ezetimibe is an intestinal cholesterol absorption inhibitor, in Type 2 DM patients, a combination of ezetimibe with lower dose of statins achieve LDL-C and non HDL-C targets more effectively than statin alone [6]. The serum levels of different lipid parameters at the time of initiating lipid lowering therapy and the pattern of prescribing lipid lowering drugs were evaluated according to the latest revised NCEP ATP III guidelines.

MATERIALS AND METHODS

A prospective observational study was conducted on patients attending the cardiology clinic of a 500 bedded tertiary care teaching hospital for duration of 6 months (January to June 2016). A detailed literature review was done. All the required study materials (informed consent document, patient information sheet, patient information leaflet and data entry form) were designed and the questionnaire SF 12 v2 for assessing the quality of life was obtained. The study was conducted only after getting approval from the IEC. The study population is a minimum of 150 patients who visited the cardiology department during the study period.

Cardiovascular patients who were diagnosed to have both diabetes and dyslipidemiaie, patients who are diagnosed with dyslipidemia and those who are already on hypolipidemic therapy, with a lipid profile of LDL-C >100mg/dl, total cholesterol >200mg/dl, HDL-C <40mg/dl and ≥60mg/dl and serum triglyceride >150mg/dl or change in any one of the above lipid parameter, as per NCEP ATP III guidelines, Patients greater than 30 years of age and Patients willing to participate were included in the study.

Patient less than 30 years of age, Pregnant Women and lactating mother and Mentally retarded were excluded from the study.

An informed consent form was taken from every patient after explanation of procedure. All the data were collected on the designed data entry form. From the 722 patients who visited the cardiology department, 165 patients who satisfied the inclusion as well as the exclusion criteria were allotted for study. The sample population was later divided in to study and reference group. Patient counselling was given only to 83 subjects in the study group. After the first review four subjects from case group and 5 subjects from control group were dropped out from study due to review failure. Then there lipid profile and prescription pattern was evaluated by NCEP ATP III guidelines.

RESULTS

PRESCRIBING PATTERN

The table no.2 and figure no.1 shows the prescribing pattern of statins in the study population. Among statins atorvastatin was prescribed for majority of patients. In the study population 96.36% (159) were prescribed with atorvastatin and 3.63% (6) were rosuvastatin.

Table 2: Prescribing pattern of statins

Table 4 : The table no.2 and figure no.1 shows the prescribing pattern of statins in the study population. Among statins atorvastatin was prescribed for majority of patients. In the study population 96.36% (159) were prescribed with atorvastatin and 3.63% (6) were rosuvastatin.

Statins	Frequency	Percentage (%)
Atorvastatin	159	96.4%
Rosuvastatin	6	3.6%

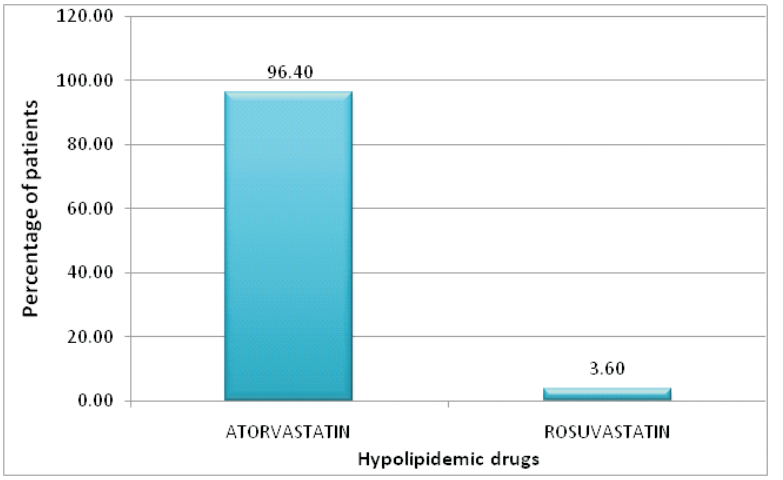

Fig 1 : Prescribing pattern of statins

Prescribing Pattern of Statins among Various Age Groups

Table No.3 shows the prescribing pattern of statins among various age groups. Maximum percentage was prescribed between the age group of 60-69 years i.e. atorvastatin 33.33% (55) and rosuvastatin, 1.81% (3) respectively. None of the patients were prescribed with rosuvastatin between 30-49 years.

Age	Atorvastatin		Rosuvastain	
	Frequency	Percentage	Frequency	Percentage
30-39	2	1.21	0	0
40-49	16	9.69	0	0
50-59	40	24.24	1	0.61
60-69	55	33.33	3	1.81
70-79	35	21.21	1	0.61
80-89	10	6.06	1	0.61
90-99	1	0.61	0	0

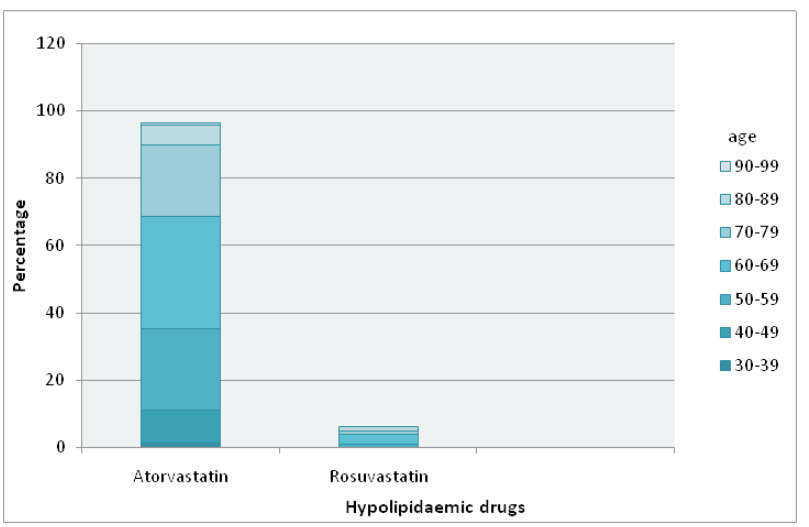

Fig 2 : Prescribing pattern of statins among various age groups

Gender wise Prescribing Pattern of Statins among the Study Population

Table No. 4 shows the gender wise prescribing pattern of statins. Among the study population, in males 66.06% (109) were prescribed with atorvastatin and 2.42% (4) with rosuvastatin. In female population 30.30% (50) were prescribed with atorvastatin and 1.21% (2) with rosuvastatin.

Gender	Atorvastatin		Rosuvastatin	
	Frequency	Percentage	Frequency	Percentage
Male	109	66.06%	4	2.42%
Female	50	30.30%	2	1.21%

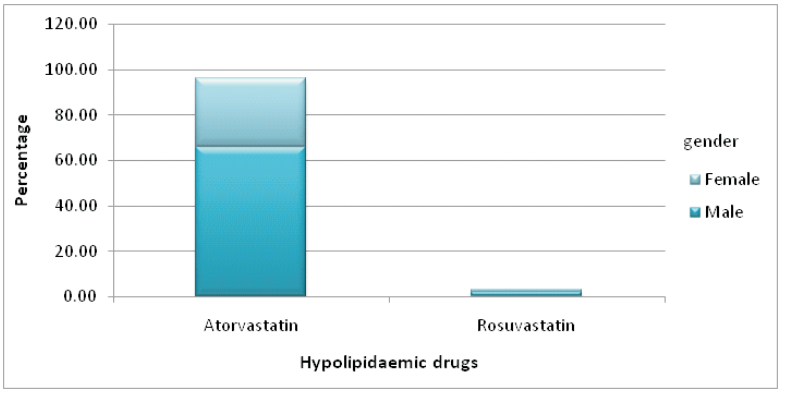

Fig 3 : Gender wise prescribing pattern of statins

Table No. 5 Statins prescribed during the hospitalization of patients

SI. NO:	DRUG CLASS	DRUG	NO.OF PRESCRIPTION	% (INDIVIDUAL DRUG)
1	STATINS	ATORVASTATIN	151	91.51
		ROSUVASTATIN	6	3.63
		ASPIRIN+CLOPIDOGREL+ ATORVASTATIN	4	2.42
		ASPIRIN+ATORVASTATIN	3	1.81
		ATORVASTATIN+CLOPIDOGREL	1	0.60

DISCUSSION

NCEP ATP III serves as a standard of care for patients with diabetes and dyslipidemia with guidelines which recommend treating dyslipidemia to LDL C and Non HDL C targets based on patient's risk of having a coronary risk in the next 10 years [8]. It is very well established that reducing LDL-C can reduce CHD events both in primary as well as secondary prevention patients [9]. As per the study conducted by Anjuprasad, In dyslipidemic patients the serum level of different lipid parameters at the time of initiating lipid lowering therapy and the pattern of prescribing lipid lowering drugs were evaluated and thus concluded that the prescribing pattern was in accordance with the NCEP ATP III guidelines [2]. Primary therapy is always directed first at the lowering elevated levels. The initial therapy is statins along with the addition of other hypolipidemic agents for the patients without previous CHD the LDLC goal is ≤ 100 mg/dl and the initiation level for pharmacological therapy is set at an LDL level≥ 130 mg/dl. According to American Diabetes Association, Diabetes Care published on January 2003 reported that elevated TG and decreased HDL cholesterol levels were the most common pattern of type 2 diabetic dyslipidaemia. It concluded that primary therapy should be directed first at lowering the elevated LDL level by statin therapy along with the addition of resin to reach the target. It also set specific goals for LDL in patients with and without CHD risk. The initial therapy for TG abnormality is improved glycemic control along with very high dose statin or fibric acid derivatives. For patients with LDL between 100 and

129 mg/dl MNT and pharmacological treatment with statin is initiated. The initial therapy of hypertriglyceridemia is always improved glycemic control along with very high dose statins (for subjects with both high LDL and TG levels) or fibric acid derivatives [10]. LDL C goals are primary target, but non HDL C was added as a secondary target for patients with hypertriglyceridemia. The optional goal of LDL C is less than 70 mg/dl for very high risk patients with established CAD, a recent acute coronary syndrome or multiple poorly controlled component of metabolic syndrome [8]. As per study conducted by SatyajitMohapatra there is a high prevalence of diabetes, as the comorbid condition for which hypolipidemic drugs were prescribed. Statin was the most common drug prescribed especially atorvastatin. Atorvastatin was given as monotherapy or in combination between aspirin. Atorvastatin was prescribed as under dosed and rosuvastatin was prescribed as overdosed [11].It is also reported in previous studies that higher dose of statin is moderately effective in reducing TG levels and were reduced need for combination therapy. With use of high dose of statin the LDL levels may be reduced to 80mg/dl. The use very high dose statin therapy (atorvastatin 40 or 80 mg) to treat hypertriglyceridemia should be restricted to patient with both high levels of LDL C and TG [10]. American Association of Clinical Endocrinologist (AACE) also recommends exercise programme and dietary changes. NCEP ATP III, AACE, ADA, ACC/AHA guidelines all recommend statin as first line agent for diabetic dyslipidemia NCEP ATP III also provide additional therapeutic information for hypertriglyceridemia. If TG are >200mg dl after the LDL C goal is achieved. Physicians either intensify the LDL C lowering therapy or add other hypolipidemic agent such as nicotinic acid or fibrates. For TG > 500 mg/dl fibrates are suggested with addition of 2 to 4 g of omega 3 fish oil. [12]

According to our study, statins were the most prescribed hypolipidemic agent and it was found to be as 100%. Out of which 96.36% were prescribed with atorvastatin and 3.63% with rosuvastatin. This is in accordance with the above guidelines.33.33% of atorvastatin was prescribed in an age group of 60-69 were our majority of dyslipidemia population was found. The majority of rosuvastatin was prescribed in the same age group and it was found to be as 1.81%. None of the patients were prescribe with rosuvastatin between 30-49 years, due to its side effect of impotency. Atorvastatin reduced the elevated LDL-C effectively with increasing the HDL-C levels. It also reduces elevated TG and other CHD events [13].

CONCLUSION

The conclusion of study exhibits that there should be early monitoring and aggressive dyslipidemia management in diabetic dyslipidemic patients. Atorvastatin was mostly prescribed as it reduces the elevated LDL-C effectively with increasing the HDL-C levels. It also reduces elevated TG and other CHD events.The evidence for preventing and treating cardiovascular disease in patients with diabetes seems conclusive. It is encouraging to see a decline in cardiovascular morbidity and mortality as a result of therapeutic interventions. Diabetes is not only treated with anti hyperglycemic agents but also with combination therapy with hypolipideamic agents aiming to reduce not only blood glucose but also to prevent or manage cardiovascular disease and other complications. The ADA guidelines state that lipid lowering with statins is a primary approach to helping reduce CVD in patients with diabetes.

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