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ORIGINAL ARTICLE

Targeted study to evaluate the cardiovascular risk factor status among patients and efficacy of statins in attaining goal lipid levels in a regional hospital in Sultanate of Oman

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Abstract *Background and objective:* Elevated LDL (Low Density Lipoprotein) cholesterol is a major cause of Coronary Heart Disease (CHD) and LDL lowering therapy reduces the risk for CHD. The study was conducted with the aim of assessing the prescribing pattern of statins based on cardiovascular risk factor category, pattern of lipid monitoring followed among the patients and extent of attainment of goal Low Density Lipoprotein (LDL-C) observed among the patients. *Methods:* A group of patient files (among those on statin agent during the year 2011) from the Department of Medicine in Nizwa Hospital were selected for targeted evaluation on the risk factor status of patients and efficacy of statins in attaining goal lipid levels. Goal LDL-C levels were estimated for each patient depending on their risk factor status. Subsequent follow ups of the patients were reviewed from the patient files and accordingly the attainment and maintenance of goal-LDL-C in the patients were evaluated. *Results:* A total of 183 patients were identified. Mean age of the evaluated patients was 63.6 ± 11.58 years. Evaluating the status of patients on the presence of risk factors, majority (63.9%) of them had presence of CHD. Simvastatin was the most commonly used agent and titration of dose was done in only 3.3% of patients. Mean LDL-C level of the patient before initiation of treatment was 3.74 ± 1.9 mmol/L. Only in 59 (32.2 %) of the total evaluated 183 patients, there was evidence of attaining goal-LDL-C levels. Among them, there was evidence

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of maintenance of goal LDL-C in 16 (27.1%) of the patients. *Conclusion:* Statins were used less frequently for primary prevention of CHD. Absence of lipid monitoring; base line and follow up in a good number of patients as well as lack of dose titration among the patients were observed. Importance of adequate lipid monitoring and follow up to ensure attainment of goal LDL-C needs to be stressed to serve the objective of use of statins; primary and secondary prevention of CHD.

1. Introduction

Research from animal studies, epidemiological studies and other shows that elevated LDL (Low Density Lipoprotein) cholesterol is a major cause of Coronary Heart Disease (CHD). LDL lowering therapy reduces the risk for CHD (Expert Panel of Detection, 2001). Guidelines recommend statins to be used for primary prevention in individuals at high risk independent of their cholesterol levels as well as for those with moderate and low risks with cholesterol levels above the threshold (Genest et al., 2009). The third report of the expert panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III, or ATP III) constitutes the National Cholesterol Education Program (NCEP) updated clinical guidelines for cholesterol testing and management. Primary goals of therapy and cut points for initiating treatment with statins are stated in terms of LDL. ATP III guidelines were formed based on large, randomized, and controlled clinical trials (RCTs) (Expert Panel of Detection, 2001). Since the publication of ATP III, 5 major clinical trials (Heart Protection Study Collaborative Group, 2002; Shepherd et al., 2002; ALLHAT, 2002; Sever et al., 2003; Cannon et al., 2004) of statin with clinical endpoints were published which resulted in the update on the guidelines (Grundy et al., 2004). Those trials confirmed the benefit of cholesterol lowering therapy in high risk patients and support the ATP III treatment goal of LDL-C < 100 mg/dl (Grundy et al., 2004). The American Diabetes Association (ADA) standards of care for diabetes state that statin therapy should be initiated in individuals with diabetes and other cardiovascular risk factors with a target LDL cholesterol of 100 mg/dl (Eldor and Raz, 2009). Statins can lower LDL cholesterol concentration by an average of 1.8 mmol/L which reduces the risk of Ischemic Heart Disease (IHD) events by about 60% and stroke by 17% (Law et al., 2003).

Previous studies have suggested that only about 1/3 of patients treated with statins actually reach the goals in primary prevention and in secondary prevention (Pearson et al., 2000). At times statins are underprescribed even among patients diagnosed with CHD (Condliffe et al., 2010). In the study conducted by Berthold to assess the patterns and predictors of statin prescription in patients with type 2 diabetes, it was reported that the majority of patients with type 2 diabetes are not receiving statins. Further, prescription was significantly higher in the secondary compared to the primary prevention group (38.1% vs. 18.5%, respectively) (Berthold et al., 2009). In the retrospective chart review conducted by Al-Siyabi et al. in Sultan Qaboos University Hospital, Oman in 2008 among 161 patients, it was observed that more than half of the high risk patients were not at the target LDL-C goals

which place them at a continuous risk of CHD (Al-Siyabi et al., 2010).

Even though statins are prescribed quite frequently in regular practice in Oman, the extent to which the efficacy of these drugs in achieving the goals of therapy (achieving target LDL-C goals) is monitored is questionable. Influence of pharmacogenomics on the efficacy of statins is documented (Mangravite et al., 2008) and hence a variation in the effect of statins in achieving the goal LDL-C is plausible depending on the genetic factors of the population. There are only limited studies conducted in Oman and in the region which tried to evaluate the efficacy or pattern of statins in achieving goal-LDL-C (Al-Siyabi et al., 2010). Monitoring of the goal LDL-C could greatly influence the efficacy of the statins in attaining the endpoints with regard to primary and secondary prevention of cardiovascular events. Hence this study was conducted with the aim of assessing the prescribing pattern of statins based on risk factor category, pattern of lipid monitoring followed among patients and extent of attainment of goal LDL-C observed among the patients. Nizwa Hospital is a 302 bed regional hospital in Al Dakhliya Governorate in Sultanate of Oman. The present study was conducted in the Department of Medicine of Nizwa Hospital.

2. Methods

The study received approval from the Regional Research and Ethics Committee of Al Dakhliya Governorate, Ministry of Health, Sultanate of Oman. A group of patient files (among those on statin agent during the year 2011) in the Department of Medicine of Nizwa Hospital was selected for targeted evaluation on the risk factor status of patients and efficacy of statins in attaining goal lipid levels. Details required for the study purpose were obtained from the patient file which included details on the statin agent used, lipid profile (before initiation of statin), assessment of the patients risk status based on the presence of CHD or CHD risk equivalents, and identification of major risk factors. In those required cases, the Framingham risk score was calculated and the risk score was categorized accordingly (Grundy et al., 2004).

Accordingly, patients were categorized into the following risk categories; Category 1 (CHD and CHD risk equivalents), Category 2 (multiple (2+) risk factors) and Category 3 (0–1 risk factor). Consequently the goal LDL-C was estimated for each patient (Grundy et al., 2004). For each case, details on the statin agent used and dose titration were obtained and evaluated. Subsequent follow ups of the patients were reviewed from the patient files regarding the lipid profiles

done. Accordingly, the attainments of goal-LDL-C in the patients were evaluated. Details on the maintenance of attained goal LDL-C were assessed. During the patient follow up period, if there was any change in risk category of the patients, accordingly the goal-LDL-C was modified for the purpose of the evaluation of the attainment of the same.

2.1. Statistical analysis

Descriptive statistical analysis was done for many of the parameters. Relationship between risk factor status and lipid profile was done by Mann Whitney U test and Kruskal Wallis test depending on the number of comparative groups. Additionally, the relationship between the patient demographics (age group and gender) with the presence of CHD and CHD equivalent was evaluated using Chi-Square analysis. P value of < 0.05 was considered to be statistically significant. SPSS version 15 was used for the statistical analysis.

3. Results

A retrospective review of the medical records was done to identify patients on any statin agent during the year 2011 (the study population) in Nizwa Hospital. Inclusion criteria for the study included data of patients who visited the outpatient department or were admitted as inpatients in the Department of Medicine and were receiving any statins in their medication list. A total of 183 patients were selected from the total of 927 patients on a statin agent.

3.1. Patient demographics

Demographics of the patients are represented in Table 1. A higher number of patients were in the age group of 61–75 (46.4%) compared to other groups. Mean age of the evaluated patients was 63.6 ± 11.58 years.

3.2. Status on presence of risk factors

Evaluating the status of the patients on the presence of risk factors, majority (63.9%) of them had the presence of CHD, Table 2. CHD equivalents such as other clinical forms of atherosclerotic disease and diabetes were present only in 28.4% of them. Diabetes mellitus was a diagnosis in 15.3% of evaluated patients. Among the 13 patients in whom the Framingham Risk Score was estimated, the average risk score was 24.07.

Table 1 Demographics of patients.

Parameters	No. (%)
Age group	
30–45	11 (6)
46–60	62 (33.9)
61–75	85 (46.4)
> 75	25 (13.7)
Gender	
Male	99 (54.1)
Female	84 (45.9)

Table 2 Status on presence of risk factors.

Parameters	No (%)
Presence of [a]CHD	
Yes	117 (63.9)
No	66 (36.1)
Presence of CHD equivalent	
Yes	52 (28.4)
No	131 (72.6)
Presence of diabetes mellitus	
Yes	28 (15.3)
No	155 (84.7)
Risk category of patients	
Category 1	169 (92.3)
(CHD and CHD risk equivalents)	
Category 2	6 (3.3)
(Multiple (2+) risk factors)	
Category 3	8 (4.4)
(0–1 risk factor)	

[a] Coronary Heart Disease.

Identifying the risk category of the patients, a vast majority (92.3%) of them belonged to category 1 (CHD and CHD risk equivalents) as represented in Table 2.

3.3. Relationship between patient demographics and risk status

The relationship between patient demographics and risk status of the patients is represented in Table 3. Accordingly, the status of the presence of CHD or CHD equivalent did not differ significantly based on the age group and gender of patients.

3.4. Details on statin agent used

Assessing the details on statin agent used among the patients, simvastatin was the most commonly used agent (86.3%) followed by atorvastatin (12.6%); Table 4. In vast majority (96.2%) of the cases, the initiating dose was 20 mg. Titration of dose was done in only 3.3% of patients. The statin agent was changed in 12% of the evaluated patients.

3.5. Details on lipid monitoring done and attainment of goal LDL-C

Details on lipid monitoring done among the patients are represented in Table 5. Only in 65.6% of patients lipid profile was obtained before initiation of statin agent. Mean/Median lipid levels among the patients are represented in Table 5.

Only in 93 patients there was a follow up lipid profile done during subsequent visits of patients. In 32.2% of the total evaluated 183 patients, there was evidence of attaining goal-LDL-C levels, Table 6. Among these 59 patients, there was evidence of maintenance of goal LDL-C in 16 (27.1%) of patients.

4. Discussion

This targeted evaluation among selected patients on statin agent was done to evaluate the risk factor status of patients, lipid monitoring pattern and attainment of goal LDL-Cs.

Table 3 Patient demographics vs. risk status.

Parameters	Presence of CHD		p value	Presence of CHD equivalent		p value
Age group	Yes	No		Yes	No	
	No. (%)	No. (%)		No. (%)	No. (%)	
30–45	3 (27.2)	8 (72.7)	p = 0.075	6 (54.5)	5(45.6)	p = 0.316
46–60	41 (66.1)	21(33.9)		17 (27.4)	45 (72.5)	
61–75	57 (67.1)	28 (22.9)		24 (28.3)	61 (71.7)	
>75	16 (64)	9 (36)		7 (28)	18 (72)	
Gender						
Male	62 (62.6)	37 (37.4)	p = 0.602	33 (33.3)	66 (66.7)	p = 0.349
Female	55 (65.5)	29 (34.5)		22 (26.2)	62 (73.8)	

Table 4 Details on statin agent used.

Parameters	No. (%)
Statin agent	
Simvastatin	158 (86.3)
Atorvastatin	23 (12.6)
Fluvastatin	2 (1.1)
Dose (mg)	
20	176 (96.2)
40	5 (2.7)
Others	2 (1.1)
Dose change	
Yes	6 (3.3)
No	177 (96.7)
Drug change	
Yes	22 (12)
No	161 (88)

Table 6 Attainment of Goal LDL-C levels.

Goal LDL-C attained	No. (%)
Yes	59 (32.2)
No	34 (18.6)
Cannot be assessed	90 (49.1)

Among the 183 patients selected for the targeted evaluation, a higher number of them were in the age group of 61–75 and were males. A similar result was obtained in the study conducted by Sreedevi et al. (2011). Current guidelines recommend the use of statins to reduce LDL-C to appropriate targets and clearly state that older age should not be a barrier to treatment (Expert Panel of Detection, 2001; Grundy et al., 2004; Wenger and Lewis, 2010). It is reported that despite evidence demonstrating clear benefit with statin therapy in older individuals, they are usually undertreated (Wenger and Lewis, 2010). Majority of the patients had CHD as a diagnosis in them. Accordingly secondary prevention was the most common indication for use. Similarly in the study conducted by Berthold et al., prescriptions for statins were significantly higher for secondary prevention than for primary (Berthold et al., 2009).

Diabetes mellitus was a diagnosis in approximately 15% of the patients. In the study conducted among 51,640 patients with type 2 diabetes in a German diabetes registry, it was observed that 34% had established atherosclerotic disease and 25.5% received a statin. Authors reported that majority of patients with diabetes mellitus are not receiving statins. Identifying the risk category of the patients in our study, vast majority (92.3%) of them belonged to category 1 (CHD and CHD risk equivalents). Prevalence of CHD did not differ significantly based on age group or gender. But, the prevalence was higher in the age groups of 46 and above. CHD is reported as the principal cause of mortality in elderly and 80% of deaths due to CHD or stroke occur in patients above the age of 65 years of age (Wenger and Lewis, 2010).

Simvastatin was the most commonly prescribed agent which was following the drug availability pattern of statin agent in the Ministry of Health, more than influenced by the choice of agents as practiced by prescribers. Atorvastatin was the most commonly used agent in the studies conducted in Indian population (Sreedevi et al., 2011; PV and Sen, 2012). The most commonly used agent, simvastatin was started on the minimum dose of 20 mg and surprisingly no dose

Table 5 Lipid monitoring and results.

Lipid profile done before initiation of statin		Lipid levels (Mean/Median)			
Yes	No	[a]TC	[b]LDL-C	[c]HDL-C	[d]TG
125 (65.6)	58 (34.4)	5.75 ([e]IQR 2)	3.74 (SD ± 1.9)	1.16 (IQR 0.46)	1.47 (IQR 1.19)

[a] Total cholesterol.
[b] Low density lipoprotein-cholesterol.
[c] High density lipoprotein-cholesterol.
[d] Triglycerides.
[e] Interquartile range.

change was observed in 96.7% of the patients. This could be explained to some extent to the fact that in 93 of the 183 evaluated patients, no follow up lipid profile monitoring was done.

According to available details, it was observed that lipid profile before initiation of statin was not obtained in 34.4% of the patients. The probable reason is that statin agent was prescribed mainly for secondary prevention irrespective of the baseline LDL-C levels. But, there is a need to obtain these base line levels in all the patients to monitor the attainment of goal LDL-C concentration after initiation of treatment. Accordingly, the lack of subsequent monitoring of lipid levels in almost 50% of the patients is a concern taking into consideration the need of monitoring the attainment of lowering of lipid levels among the patients. In the meta analysis conducted by Law et al. aimed at quantifying the effect of statins on LDL-C levels in IHD and stroke, it was reported that statins can lower LDL-C concentration by an average of 1.8 mmol/L which reduces the risk of IHD events by 60% and stroke by 17% (Law et al., 2003).

Mean LDL-C of the patients before initiation of the statin agent was 3.74 ± 1.9 mmol/L. These values were lower than the pretreatment concentration of LDL-C reported in the meta-analysis by Law et al. which was 4.8 mmol/L (Law et al., 2003).

4.1. Limitations

The study had its own limitations. As it is based on retrospective data like any other study relying on already available data, inherent drawbacks of incomplete or inconsistent documentation could be expected. As vast majority of the patients were only on simvastatin, a reliable data on the effect of other agents could not be assessed. Further, only in 50% of the patients, follow up lipid profile was available and accordingly attainment of goal LDL-C could not be assessed. Further, since the follow up lipid monitoring was done at different time durations after initiation of statin in the patients, generalized quantification of the time taken for reduction in lipid levels among the patients could not be done effectively.

5. Conclusion

The study was able to provide certain useful information on the prescribing pattern of statins based on risk factor category, pattern of lipid monitoring followed among the patients and extent of attainment of goal LDL-C observed among the patients. Considering the risk factor category of statin users, it was most commonly used for category 1 patients (CHD and CHD equivalents) and secondary prevention of CHD. It was used for primary prevention less frequently and was used in patients with diabetes mellitus also less commonly. Absence of lipid monitoring; base line and follow up in a good number of patients as well as lack of dose titration among the patients were observed. Attaining of goal- LDL-C among the statin users is of prime importance and the evidence of the same was observed only in one third of the evaluated patients. Adequate lipid monitoring and follow up to ensure attainment of goal LDL-C will serve the purpose of statin use; primary and secondary prevention of CHD.

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