

Research Article

Evaluation of Prescription Pattern, Adverse Drug Reaction and Cost Analysis of Anti-Hyperlipidemic Drugs

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ABSTRACT

Hyperlipidemia ought to be the prominent cause of all Cardio Vascular Diseases (CVD). Evidence-based guidelines issued by the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) underlines the importance of hyperlipidemia treatment with an aggressive LDL-C goal of <100 mg/dl for high risk patients. For the reduced cardiovascular morbidity and mortality the lipid lowering drugs ought to be given on a long-term basis. But on the other hand, incidence rate shows that these agents especially statins found to have many risks on long term use, which was the reason to have a look on it. The aim of the present study was to assess the risk of using statins on a long term basis and the burden caused by the same in the patients. A total of 105 patients of ≥ 26 years of age were collected. Among that 55 were males and 50 were females. Commonly prescribed anti-hyperlipidemic drug was atorvastatin. 6 ADRs were found in the present study. The major one was rhabdomyolysis followed by muscle pain, elevated creatinine kinase and transaminase. The ADRs found were assessed by Naranjo's probability scale and Hartwig's severity assessment scale. The cost analysis of these drugs was done on the basis of duration of hospital stay for the burden caused. Descriptive analysis was the statistical method used. The present study gave a better knowledge on the risk of statins, which on long term use may lead to lethal effects like kidney and liver failure.

Keywords: Hyperlipidemia, Anti-hyperlipidemic drugs, Naranjo's probability scale, Cost Analysis.



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INTRODUCTION

Hyperlipidemia is presumably the major risk factor for cardiovascular morbidity and mortality and its treatment has come to the forefront for its preventative strategy.¹ The safety profile of all the drugs need to be monitored before they enter in to the market which is the post marketing surveillance period. Adverse drug reactions are often considered to be the possible reason for hospital admissions.²

Statins are the drug of choice for hypercholesterolemia and diseases pertaining to cardiovascular system. These drugs are currently the most frequently used and best selling prescription drug worldwide.³ Due to their

efficacy, there is a widespread use of statins for broad populations and for which number of generic forms are available.⁴ Since statins are prevalent in use, it is imperative to understand the risks involved with taking these medications. Known adverse events with statin therapy ranges from raised liver enzymes to potentially fatal rhabdomyolysis. Musculoskeletal complaints are very common with statins.

Due to the potential adverse effects and underutilization of these drugs physicians may often deter to prescribe these medications.⁵ Asymptomatic mild elevation of serum transaminases (often self-limiting) have been

reported with all statins with varying incidence. Hepatotoxic effects are considered to be the potential effects of statins along with myopathy having a due attention.³ Recently ezetimibe has been viewed as a safe alternative to statin therapy in the setting of pre-existing liver disease.¹ By considering the above facts we have evaluated this study on prescription pattern, ADRs and cost of anti-hyperlipidaemic drugs.

METHODS

A Prospective Observational Study was conducted at General Medicine in-patient department of Basaveshwara Medical College Hospital & Research Centre, Chitradurga. The study was conducted for a period of six months and was approved by the "Institutional Human Ethical Committee" (SJMCP/IEC/54i/2014-15 Date 13/10/2014) of the S.J.M College of Pharmacy, Chitradurga. All the patients who were presented to general medicine in-patient department with anti-hyperlipidemic medication during the study were eligible for enrollment. Pregnant and lactating mothers and psychiatric patients were excluded from the study. The data was collected through patient interviews and from medical records of the patient. Obtained patient information was documented in a suitably designed Individual Case Record Form (ICRF). Identified adverse drug reactions associated with anti-hyperlipidemic drug usage and assessed by using Naranjo's Causality Assessment Scale and defined the severity of ADRs using Hartwig's severity assessment scale. Cost analyses of anti-hyperlipidemic drugs were done on the basis of duration of hospital stay. All the enrolled patients were monitored from the date of admission until discharge for any occurrence in adverse drug reactions and change in drug therapy.

Statistical analysis:

The study was based on descriptive analysis. The data was entered in Microsoft excel 2010 version and the results were analyzed using Statistical Package for Social Service (SPSS) 16 version, the results were calculated and analyzed qualitatively by Chi square test.

RESULTS AND DISCUSSIONS

A total of 105 prescriptions were collected from the general medicine in-patient department of Basaveshwara Medical College Hospital & Research Centre, Chitradurga. Among whole 50 were females and 55 were males. Out of 105, 15 patients were from 26-46 age group, 58 patients were from 47-66 age group and 32 patients from 67-86 age group. The P-value (0.1-NS) and the chi-square test value is $X^2=4.6$.

Anti-hyperlipidemic drug therapy:

Out of the 105 prescriptions of anti-hyperlipidemic drug therapy, 67(63.2%) prescriptions were found to be of Atorvastatin and 38(35.8%) prescriptions were of Aspirin + Atorvastatin. Statins(HMG-CoA reductase inhibitors) were the only prescribed class.

Distribution according to duration of hospital stay:

Duration of hospital stay was relevant in assessing the cost of the medication. The cost analysis per prescription was calculated according to the number of days stayed in hospital (table.1) and the patients were followed from the date of admission to the date of discharge for any change in drug therapy as well as for the occurrence of adverse drug reactions.

Distribution according to adverse drug reactions and suspected anti-hyperlipidemic drugs:

In the present study a total of 6 ADRs have occurred which was due to Atorvastatin. Rhabdomyolysis was seen in 2 patients(40%) followed by transaminase elevation(20%), CPK level elevation(20%), muscle pain, lower back pain and difficult urination(20%) as shown in table.2. Muscle related problems are more common with statins. In severe case it leads to rhabdomyolysis.

Causality Assessment of ADRs by using Naranjo's Probability Scale:

The ADRs occurred has been assessed by using Naranjo's Probability scale. The ADRs documented probable as 1 and possible 4 only. No definite and doubtful ADRs were found as shown in table no.3.

Assessment of Severity of ADRs by using Hartwig's Scale:

All the ADRs occurred were assessed by Hartwig's severity assessment scale. The ADRs documented as mild 2 & moderate 3. No severe ADRs were found as shown in table.No 3.

Cost of anti-hyperlipidemic drugs:

It was one of the important objective of our project to assess the direct cost of anti-hyperlipidemic drugs. The cost analysis was done per prescription. The duration of hospital was taken into account. Cost analysis is usually done to know the burden caused to the patient by the treatment. Tabulating the expenditure of inpatient's on antihyperlipidemic drugs during the hospital stay it shows as in table 4.

Table 1: Distribution according to duration of hospital stay

Duration of hospital stay	patients	Percent %
<2 days	5	4.7
3-5 days	55	51.9
6-8 days	40	37.7
>8 days	5	4.7
Total	105	99.1

Suspected drug	ADRs experienced	No. of patients	Percent%
Atorvastatin	Lower back pain, difficult urination	1	20
	Muscle pain, CPK Level elevated	1	20
	Transaminase level elevation	1	20
	Rhabdomyolysis	2	40
Total	6	5	100

Table 2: Distribution according to adverse drug reaction and suspected anti-hyperlipidemic drugs

Naranjo's causality scale	assessment		Hartwig's severity assessment scale		
	Causality assessment	No. of ADRs	Percent%	Severity assessment	No. of ADRs
Definite(>9)	0	0	Mild	2	40
Probable(5-8)	1	20	Moderate	3	60
Possible(1-4)	4	80	Severe	0	0
Doubtful(0)	0	0			
Total	5	100%	Total	5	100%

Table 3: Causality and Severity assessment of Adverse Drug Reactions

Duration of Hospital stay	No. of Patients	Average cost of anti-hyperlipidemic drugs per day	Average cost of anti-hyperlipidemic drugs during hospital stay
1-2	5	9.72	42.97
3 to 5	55	10.44	45.74
6 to 8	40	9.4	63
>8	5	5.14	48.98

Table 4: Expenditure of antihyperlipidemic drugs during the hospital stay

DISCUSSION

Decades of research has demonstrated a causal relation between high total cholesterol levels, specifically with increase in low-density lipoprotein cholesterol (LDL-C).⁶ But there has been a very little change in total cholesterol levels in more than a decade despite public awareness campaigns to reduce cholesterol.⁷ The newest Adult Treatment Panel guidelines of the National Cholesterol

Education Program(ATP III) identifies the optimal LDL lower than previous reports and recommends even more aggressive management in patients with a coronary heart disease risk equivalent.⁸ Amir Kashani et al.,conducted a study on Risks associated with statin therapy: A Systematic Overview of Randomized Clinical Trials. Among 74102 subjects enrolled in 35 trials statin therapy (excluding cerivastatin) did not result in significant

absolute increase in risks of myalgias, creatine kinase elevations, rhabdomyolysis. The absolute risk of transaminase elevations was significantly higher with statin therapy. The study concluded that statin therapy is associated with a small excess risk of transaminase elevations, but not of myalgias, creatine kinase elevations, rhabdomyolysis.⁹ The present study found 6 ADR's which include lower back pain, difficult urination, muscle pain, CPK Level elevation, Transaminase level elevation, Rhabdomyolysis. The absolute risk of rhabdomyolysis was significantly higher with statin therapy in our study.

Wagner M *et al.*, conducted a study on Cost-effectiveness of intensive lipid lowering therapy with 80 mg of atorvastatin, versus 10 mg of atorvastatin, for secondary prevention of cardiovascular disease in Canada. The results shows that treatment with atorvastatin (80 mg) over a lifetime horizon resulted in increased costs, survival and QALYs per patient compared with atorvastatin (10 mg), yielding an incremental cost-effectiveness. They concluded that Intensive atorvastatin (80 mg) treatment is predicted to be cost-effective versus atorvastatin.¹⁰ In the present study also 80mg atorvastatin (Rs 198 per strip) found to be more costlier than 10mg atorvastatin (Rs 25 per strip).

Limitations of the study:

- The sample size was less due to shorter duration of study period.
- Limitation of pharmacoeconomical study to only direct cost due to lack of time.
- Few numbers of anti-hyperlipidemics prescribed which limited the study to a particular class of drugs.

Future directions:

- Large sample size will give still more precise and accurate results.
- Conduction of the study for longer duration of time.
- The pharmacoeconomical study can be done for both direct and indirect cost.

Our study concludes that statin therapy on long term use may often leads to adverse effects in some patients and if left unnoticed these adverse effects can lead to fatal effects like rhabdomyolysis, kidney and liver failure. Here comes the responsibility of a pharmacist to identify and monitor those reactions for a better patient care. To facilitate efficient and effective management of patients with dyslipidemia

the cost effectiveness also plays an important role apart from monitoring adverse drug reactions. Some drugs are expensive and the patient finds difficult to adhere with the treatment. At this point the pharmacist should understand which therapy is cost effective for the individualized patient.

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