EFFICACY OF ATORVASTATIN IN REDUCING PROTEINURIA IN PATIENTS OF CHRONIC KIDNEY DISEASE

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ABSTRACT

Objective: To determine the efficacy of atorvastatin in reducing proteinuria in patients of chronic kidney disease.
Study Design: Quasi experimental study.
Place and Duration of Study: Combined Military Hospital Multan, from Jan 2014 to Jun 2014.
Material and Methods: Seventy patients of both genders with documented chronic kidney disease (GFR <90 >15ml/min) for at least 3 months duration were included by non-probability consecutive sampling. Age of the patients and reduction in proteinuria from the baseline after using atorvastatin was noted. The data were analyzed by using SPSS v 19. Descriptive statistics like mean ± SD, percentages and frequencies were calculated for age and efficacy of atorvastatin. The data collected for study was statistically analyzed using chi-square test.
Results: The overall efficacy of atorvastatin was 31.43%. Twenty two out of 70 subjects had significant reduction in proteinuria i.e.>0.25 gm/24 hrs from baseline after statin use. A significant statistical association was not seen in the efficacy of atorvastatin between males and females, *p*-value being >0.05.
Conclusion: A notable number of patients had improvement in their 24 hours proteinuria after the use of atorvastatin. Therefore atorvastatin use may be beneficial in all patients of chronic kidney disease as it will reduce progression of the disease and prevent rate of decline in renal functioning.

Keywords: Atorvastatin, Chronic kidney disease, Efficacy, Proteinuria.

INTRODUCTION

Chronic kidney disease (CKD) is one of the major health problems resulting in a significant increase in morbidity and mortality as well as decreased quality of life and significant health care expenses[1]. Proteinuria in chronic kidney disease is associated with increased morbidity and mortality. It is a biomarker of progression of chronic kidney disease as well as a mediator of this destructive disorder[2]. Angiotensin-converting enzyme (ACE) inhibitors and statins are helpful in reducing micro-albuminuria and cardiovascular risk in these patients of (CKD) especially those with cardiovascular involvement[3].

Hyperlipidemia not only contributes to cardiovascular diseases but has also been identified as an independent risk factor for the progression of chronic kidney disease[4]. Various studies highlight the processes contributing in lipid induced kidney damage where multiple mechanisms are involved but the inciting event by hyperlipidemia is present[5]. Few intervention studies in a variety of animal models have analyzed the role of statins on reducing kidney damage[6]. Statins are competitive inhibitors of HMG CoA reductase enzyme, the rate limiting step in cholesterol biosynthesis[7]. By their lipid lowering action they play a vital role in prevention of coronary heart disease. But statins also have a protective effect on kidney structure and function[8]. Not only statins reduce proteinuria, they reduce inflammatory processes and prevent histological changes of inflammation and fibrosis in the kidney[9]. In an international study there is 29% decrease in progression of chronic kidney disease after the use of atorvastatin[6] and in another study there was 20% reduction in proteinuria after use of atorvastatin[10].

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Normal individuals demonstrate a reduction in renal function with age. Above the age of 30 years, this amounts to an average decrease of 0.7 to 0.9 mL/min in the glomerular filtration rate (GFR) per year. Once renal injury has started, the decline in GFR can be accelerated by hypertension, proteinuria, as well as by dyslipidemia.The rate of decline in GFR in established chronic kidney disease (CKD) can be decreased with early intervention[11]. The most successful intervention is control of elevated blood pressure and there may be an added benefit of using angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers especially in those with significant proteinuria[12].

According to some animal studies, hyperlipidemia is usually associated with glomerular injury[13], which leads to glomerulo-sclerosis. However, it does not show a relationship with human studies in which lipid-rich conditions such as familial hyperlipidemia, do not seem to lead to clinically-relevant renal injury. Perhaps this is due to earlier development of significant cardiovascular disease or targeted interventional therapy. On the other hand, if (CKD) has started, small series of studies have shown an association between progression of renal disease and hyperlipidemia[14,15]. The objective of the study was to determine the efficacy of atorvastatin in reducing proteinuria in patients of chronic kidney disease. The results of our study might have important clinical/therapeutic implications on clinical treatment of patients with CKD.

MATERIAL AND METHODS

A quasi experimental study was conducted, from January 2014 to June 2014 at General Medicine Departments of Combined Military Hospital Multan (CMH) with confidence level 95%, anticipated population 22%[4], absolute precision 10%. A sample size of 70 patients was calculated using WHO calculator. Seventy Patients aged between 18 to 75 years of both genders with documented chronic kidney disease (GFR <90>15ml/min) for at least 3 months were included via non-probability consecutive sampling. Patients showing reduction in proteinuria of 0.25 gm/24 hrs from their baseline was considered as significant. Patients excluded from the study were those with acute liver disease ALT >300 U/L, patients already on statins or hypersensitivity to atorvastatin, patients on renal replacement therapy.

Permission was obtained from "Hospital Ethical Committee". About 70 patients were selected considering inclusion and exclusion criteria. Written informed consent was obtained from the study participants after introducing them to the study objectives and possible side effects of atorvastatin like muscle pain, jaundice, difficulty sleeping, abdominal pain. Queries regarding the study were answered thoroughly. Patients were explained in detail how to collect sample for 24 hour urine. Name, age and hospital ID number were entered in the proforma. Participants were ensured that the information taken shall be used solely for research purposes.

Blood Complete picture, renal function tests, fasting lipid profile, 24 hour urinary protein were carried out initially as base line reference and then after the usage of atorvastatin 10mg daily at night for two months and reports were collected personally. All the necessary information was entered in the proforma. To ensure follow up contact numbers of patients were noted.

All data collected were entered in SPSS version 19.0. Descriptive statistics, mean and ± standard deviation were calculated for quantitative variables like age of the patient, pre and post treatment proteinuria. Qualitative variables like gender and efficacy are presented as frequency and percentages. Results are presented with the help of tables and charts. A statistical analysis was done using chi-square test to compare the efficacy of atorvastatin between males and females. A p-value ≤0.05 considered as a significant value.

RESULTS

Out of Seventy patients fulfilling inclusion/ exclusion criteria there was significant reduction in proteinuria of >0.25 gm/24 hrs from baseline

in 22 patients using 10 mg of atorvastatin/day. So the overall efficacy of atorvastatin was 31.43%. Out of those 22 patients,15 were males and 7 were females. In 48 pts there was reduction in proteinuria which was less than 0.25 gm/24 hrs or there was no reduction in proteinuria. No significant side effects were noted in any patient after 02 months usage of atorvastatin. A significant statistical association was not seen in the efficacy of atorvastatin between males and females, *p*-value being >0.05.

Age distribution was done which shows that mean age was 52.19 with standard deviation of 12.744 (table-I).

Gender distribution of the patients was done which shows that 31.42% (n=22) were females and 68.57% (n=48) were males (table-II).

Table-I: Age distribution (n=70).

	Minimum	Maximum	Mean ± SD
Age (years)	18	75	52.19 ± 12.744

Table-II: Gender distribution of atorvastatin efficacy (n=70).

Gender	Frequency (%)		Total (%)
	Females	Males	
Efficacy	7 (10)	15 (21.42)	31.43
No efficacy	15 (21.42)	33 (47.14)	68.57

In the study, 31.43% (n=22) showed significant reduction in proteinuria while 68.57% (n=48) showed no significant reduction in proteinuria after using atorvastatin (figure).

DISCUSSION

In this study 10mg atorvastatin was given to 70 patients of CKD, mean age of 52 years, irrespective of the underlying cause of the disease for 02 months. Patients initial proteinuria over 24 hours was noted and then again after 2 months. Results of our study clearly identify reduction in protienuria by >0.25gm/24 hrs in 31.43% of the patients.

As compared to other studies conducted worldwide to assess effects of statins in patients with chronic kidney disease meta-analysis and meta-regression of randomized controlled trials[10-15], showed a significant reduction in 24 hour urinary protein excretion (g/24h) in chronic kidney disease (pre-dialysis). Patients receiving statins compared with placebo in 6 randomized controlled trials, 311 patients showed weighted mean difference (0.73g/24hrs, 0.95 to 0.52)[4], our study also showed similar results but study group is smaller and duration of study is less. Similarly in a Planet II study[10], conduted on diabetic patients, deZeeuw concluded that Atorvastatin prominently decreased the pro-teinuria in these patients on top of ACE/ARB therapy, with approximately 15% decrease in proteinuria, whereas rosuvastatin, both 10 and 40mg, had no similar effect at all on proteinuria. Similar results were noted in a Planet II[5] study conducted on non-diabetic cohort in which a similar pattern was observed, even more significant. Atorvastatin caused reduction in proteinuria by >20% at the end of 26 & 52

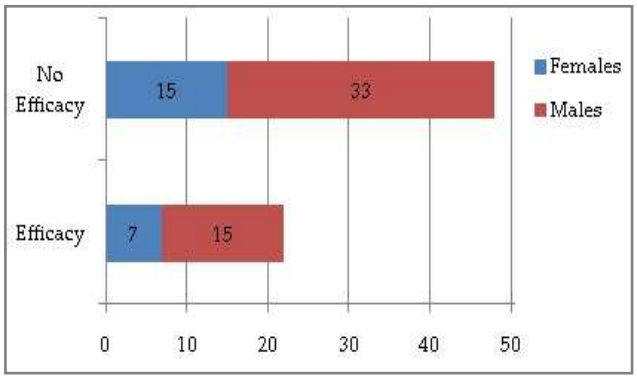

Figure: Relative efficacy of atorvastatin.

weeks of the study, however there was no prominent effect noted with rosuvastatin.

Results pertaining to albuminuria were nearly identical to those for proteinuria. The results of our study highlighted that the overall efficacy of atorvastatin was 31.43% and it shows that in patients of chronic kidney disease, atorvastatin is significantly useful in reducing proteinuria. Our study lacks the assessment of effects of different statins on proteinuria in comparison with each other that which of the statin is most effective in reducing proteinuria. It is also important to note that efficacy of atorvastatin was studied over two months period for each patient. The

effects and side effects of the drug may take longer time to become manifest in different patients.

The study also showed the benefit of using 10mg/d atorvastatin to the noncardiac benefits of statins in patients of chronic kidney disease. Decrease in proteinuria by atorvastatin seems to maximize renal benefits in high risk patients and shall be used in moderate CKD. The findings from this study are fascinating and when considered along with previous statin clinical trials, may have important clinical/therapeutic implications on clinical treatment of patients with CKD.

Different studies indicate significant reduction in proteinuria after the use of different lipid lowering agents[16,17]. In one study it revealed statins appear to decrease the rate of reduction of eGFR and slow the progression of pathologic proteinuria moderately[18]. It is required that studies should be performed to compare the effect of different statins with each other. Studies should be done to assess whether statins are helpful in patients on hemodialysis or patients of end stage renal disease. Studies need to be done to identify if atorvastatin or any other statin can delay development of proteinuria in patients of chronic kidney disease who haven't developed proteinuria and for how long development of proteinuria can be delayed. Cross benefit analysis of efficacy and side effects of prophylactic use of statins may also be studied.

CONCLUSION

A notable number of patients showed improvement in their 24 hrs proteinuria after the use of atorvastatin. Therefore atorvastatin use may be beneficial in patients of chronic kidney disease as it will reduce progression of the disease and prevent rate of decline in renal functioning.

It is recommended that astorvastatin 10mg daily be given to all patients of CKD.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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