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Comparison of the effect of atorvastatin and aspirin on C-reactive protein concentration in hemodialysis patients

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Abstract

Introduction: Chronic inflammation is one of the underlying causes of cardiovascular disease which is commonly seen in patients with chronic kidney disease (CKD) and especially in end-stage renal disease (ESRD), as well as the patients on stable dialysis. Hemodialysis patients suffer from high mortality due to cardiovascular diseases.

Objectives: Therefore, the present study aimed to evaluate the effect of atorvastatin and aspirin on C-reactive protein (CRP) concentration in hemodialysis patients and compare the effect of these two drugs on CRP concentration in these patients.

Patients and Methods: In this descriptive-analytical study, the dialysis patients who had been on dialysis for more than four months were selected through medical records (N=75). Serum CRP was checked and those who had positive CRP entered in the analysis (n=20). Ten patients had been used atorvastatin at a dose of 20 mg daily and the other 10 patients received aspirin at a dose of 80 mg daily for two months. Serum CRP concentration was measured in all patients at the end of these two months.

Results: The mean age of the patients was 65.6 years and the mean number of years on dialysis was three years. In addition, 65% of patients were male and 35% were female. The only significant relationship was between the effect of atorvastatin and CRP concentration and the effect of aspirin on CRP concentration while no statistically significant relationship was found between the two groups of aspirin and atorvastatin in terms of serum CRP value after the intervention.

Conclusion: The results indicated that the effect of aspirin and atorvastatin on CRP concentration was positive in hemodialysis patients and reduced the serum level of CRP, indicating the anti-inflammatory role of these two drugs in hemodialysis patients. It should be noted that drug preference was not determined in the present study.

Keywords: End stage renal disease, Hemodialysis, Inflammation, C-reactive protein, Atorvastatin, Aspirin

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Introduction

Chronic kidney disease (CKD) includes a range of various pathophysiological processes with abnormal kidney function (1,2). The last stage of CKD is end stage renal disease (ESRD), where the accumulation of toxins, fluids and electrolytes which are normally excreted by the kidneys causes uremic syndrome. Such a syndrome results in death unless the toxins are removed out of the body using kidney replacement therapy through dialysis or a kidney transplant (3,4).

The incidence of ESRD is 330 cases per one million people per year, which is heterogeneously higher among the black people than the white people (5). Based on the center for transplantation and special diseases management (MCTSD) of Iran, the prevalence and incidence of ESRD in Iran has increased significantly during the recent years and kidney transplantation and hemodialysis are the most common alternative kidney treatment methods used in Iran (6). The patients on stable dialysis have some complications such as hypotension, muscle cramps, and high mortality because of cardiovascular disease (7-9). The most significant pathophysiology involved in the phenomenon of inflammation is the acute phase response. One of the acute phase proteins is C-reactive protein (CRP), which increases during the inflammatory process in plasma in different diseases, including CKD and dialysis (10,11). Statins are the structural analogues of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-COA). Lovastatin, atorvastatin, fluvastatin, pravastatin, simvastatin and rosuvastatin belong to this category (12,13). These drugs are the most effective in decreasing low-density lipoprotein (LDL), reducing oxidative stress, and vascular inflammation related to atherosclerotic lesions (14,15). Aspirin or acetylsalicylic acid with the molecular formula

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Implication for health policy/practice/research/ medical education

Atorvastatin and aspirin both had a positive effect on C-reactive protein (CRP) concentration and decreased the serum level of CRP, indicating the anti-inflammatory role of these two drugs in hemodialysis patients.

C9H8O4 is an aromatic compound which has a benzene ring in its structure and belongs to non-steroidal anti-inflammatory drugs (16,17). Such drugs have antipyretic and anti-inflammatory effects and decrease the incidence of transient ischemic attacks, unstable angina, coronary artery thrombosis with myocardial infarction and thrombosis (18,19). Cardiovascular disease is a main cause of death in ESRD patients and dialysis patients. The underlying cause of cardiovascular disease is not known yet, but chronic inflammation can be mentioned as one of the underlying causes. Since statins and aspirin are effective drugs in reducing oxidative stress and vascular inflammation and since the effect of atorvastatin and aspirin on the CRP concentration of hemodialysis patients has not been studied.

Objectives

This study aimed to describe the effect of aspirin and atorvastatin on CRP concentration in hemodialysis patients and compare the effect of these two drugs on CRP concentration in these patients.

Patients and Methods

Study design

Research population and sample size

In this descriptive-analytical study, the hemodialysis patients of Hajar hospital in Shahrekord and Valiasr hospital in Borujen, as well as Seyed Shohada hospital in Lordegan were selected in August, September, October and November 2011. In addition, 20 hemodialysis patients from Hajar hospital in Shahrekord and Seyed Shohada in Lordega, as well as interns and dialysis ward staff were selected. Twenty dialysis patients who had been on dialysis for more than four months taking aspirin and atorvastatin were selected through medical records

CRP concentration was measured for all patients. Ten patients had been used atorvastatin at a dose of 20 mg daily and the other 10 patients received aspirin at a dose of 80 mg daily for two months. The study was conducted with the permission of the university vice chancellor for research.

Statistical analysis

After collecting the information and recording it in the predetermined checklist, Mann-Whitney U test and Wilcoxon signed-rank test were used through SPSS version 19 (SPSS Inc., Chicago, IL, USA). Pearson's correlation coefficient was used to investigate the relationship between continuous quantitative data. A P value ≤0.05 was significant.

Results

Of 20 dialysis patients in the present study, 65% were male and 35% were female. The mean age of patients was 65.6 years (ranging from 41 to 89 years).

The mean duration of dialysis was three years (ranging from 1 to 8 years). The cause of kidney failure was different in the patients: Furthermore, seven subjects had diabetes, six subjects had hypertension, three subjects had nephrolithiasis, two subjects had both diabetes and hypertension, and one subject had polycystic kidney and one also had bilateral nephrectomy. The results of Mann-Whitney U test showed no significant difference regarding age, serum CRP and duration of dialysis for aspirin and atorvastatin groups across genders ($P > 0.05$; Table 1).

Due to the small sample size and non-normal distribution assessed by histogram, the non-parametric Wilcoxon Signed ranks test was conducted, which was significant both for aspirin ($P = 0.04$) and for atorvastatin ($P = 0.004$) as a result of the effect of the drugs on serum CRP between male and female patients (Table 2).

Using the Mann-Whitney U test to compare the two groups in respect of CRP, the two groups were not

Table 1. Relationship between studied variables in groups by gender

Group	Variable	Gender	Mean ± SD	*P* value
Aspirin	Age (year)	Male	62.29±13.91	0.568
		Female	67.0±7.0	
	Number of dialysis (year)	Male	2.75±2.71	0.715
		Female	2.67±1.53	
	Baseline CRP (mg/L)	Male	39.24±38.86	0.189
		Female	13.33±2.31	
Atorvastatin	Age (year)	Male	64.33±11.64	0.831
		Female	67.75±15.86	
	Number of dialysis (year)	Male	3.67±2.58	0.382
		Female	2.87±2.75	
	Baseline CRP (mg/L)	Male	33.66±28.0	0.360
		Female	39.31±37.50	

CRP, C-reactive protein.

significantly different at baseline and two-month follow up (Table 3; $P>0.05$).

The results of the effect of drugs between CRP and the duration of dialysis and age revealed no statistically significant correlation (Table 4; $P>0.05$).

Discussion

A study on 1702 males and females with no history of cardiovascular disease and another study on 1182 males and females with a positive history of cardiovascular disease concluded that statin with a daily dose of 40 mg for 12-24 weeks had anti-inflammatory effects (20). Another study showed that statin had anti-inflammatory effects on atherosclerotic plaque formation and cell function in patients with coronary artery disease (21). In addition, another study indicated that prescribing 20 mg simvastatin significantly reduced serum CRP and interleukin 6 (IL-6) levels and white blood cell counts in dialysis patients and prescribing simvastatin to dialysis patients was safe (22). Furthermore, a study on 5742 patients about the effect of lovastatin treatment to prevent the primary vascular events and CRP levels indicated that treatment with lovastatin for 20 mg daily during 12 weeks reduced CRP levels and prevented primary vascular accidents among the people with high CRP levels (23). Another study which was conducted on 20 patients with hyperlipidemia checked serum lipids and CRP and gave atorvastatin 10 mg/d for three months, and immediately the tests were repeated again after three months when a significant reduction in serum LDL-c and CRP was observed (24). The present study indicated that atorvastatin in hemodialysis patients at a dose of 20 mg daily for two months reduces the concentration of CRP and has anti-inflammatory effects with this dose and the duration of treatment in these patients. In a study evaluating the role of aspirin in CRP levels in 543 males with MI or ischemia but no venous thrombosis, the results revealed that aspirin reduced serum CRP levels and the risk of heart attack with aspirin (25). In another study on 121 patients with metabolic syndromes, it was shown that aspirin for two weeks and 100 mg daily for two weeks reduced the CRP levels (26). In addition, the present study showed that in hemodialysis patients who took aspirin (at a dose of 80 mg daily for two months), there was a decrease in serum CRP concentration and aspirin at this dose and the length of treatment in these patients had anti-inflammatory effects in these patients.

Conclusion

The results of the present study indicated that atorvastatin and aspirin both had a positive effect on serum CRP concentration and decreased the serum level of CRP, indicating the anti-inflammatory role of these two drugs in hemodialysis patients. It should be noted that drug preference was not specified in the present study.

Limitations of the study

In our study, it was found that both aspirin and atorvastatin have a positive effect on CRP levels in hemodialysis patients, but since the preferred type of drug is not known,

Table 2. The effect of aspirin and atorvastatin on CRP by gender

Group	Gender	Baseline CRP (mg/L)	Two-month follow up CRP (mg/L)	*P* value
Aspirin	Male	39.24±38.86	11.43±11.18	0.040
	Female	13.33±2.31	3.46±3.0	
Atorvastatin	Male	33.66±28.0	6.53±2.67	0.004
	Female	39.31±37.50	6.0±3.0	

CRP, C-reactive protein.

Table 3. Comparison of the two groups before the intervention on the CRP mean

Variable	Group	Mean ± SD	*P* value
Baseline CRP(mg/L)	Aspirin	31.80±34.18	>0.999
	Atorvastatin	31.20±34.34	
Two-month follow up CRP(mg/L)	Aspirin	2.8±5.97	0.155
	Atorvastatin	7.6±9.08	

CRP, C-reactive protein.

Table 4. The effect of intervention on CRP correlation and number of dialysis and age

Variable	Group	Baseline CRP, correlation, (*P* value)	Two-month follow up CRP, correlation, (*P* value)
Duration of dialysis (year)	Aspirin	-0.316 (0.374)	0.254 (0.478)
	Atorvastatin	-0.301 (0.398)	-0.368 (0.324)
Age (year)	Aspirin	0.145 (0.688)	-0.425 (0.221)
	Atorvastatin	-0.023 (0.949)	-0.69 (0.849)

CRP, C-reactive protein.

it is suggested that these two drugs be checked in a study with larger sample size.

Authors' contribution

Conceptualization, methodology, visualization, supervision, project administration: SM.
Validation, data curation: MA.
Formal analysis, resources: BS.
Investigation: SN.
Writing—original draft preparation, writing, review and editing: MM.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Shahrekord University of Medical Sciences approved this study. (#IR.SKUMS.REC.1389.610). Accordingly, written informed consent was taken from all participants before any intervention. Besides, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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