International Journal of Research in Medical Sciences
Egboh SC et al. Int J Res Med Sci. 2018 Oct;6(10):3259-3263
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20184028

Original Research Article

Effects of statins on the c-reactive protein of dyslipidemic patients in the university of Port-Harcourt teaching hospital

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Received: 24 July 2018
Accepted: 29 August 2018

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ABSTRACT

Background: Dyslipidemia is a modifiable cardiovascular risk factor associated with systemic inflammation and can be assessed with a recognized bio-marker known as C-reactive protein.
Methods: This was a cohort study carried out over a period of 9 months, where subjects who had abnormality in any of the fasting lipid parameters were recruited into the study, all the subjects had their C-reactive protein assessed, the test subjects were commenced on statins while the control subjects were not on statins and they were all followed up for a period of 3 months after which C-reactive protein was re-assessed.
Results: Total 320 subjects were recruited, comprising of 160 test subjects and 160 control subjects. The mean age± SD of the test subjects was 57.02±12.45, while the control subjects had 51.86±13.27 as their mean age± SD. Statins had a significant effect on the reduction of C-reactive protein (p=0.001). Although, there was no correlation between the dosages of statins and its effect on C-reactive protein.
Conclusions: Statins were found to have anti-inflammatory effects, although there was no significant correlation between the dosages of statins and their effect on c-reactive protein.

Keywords: Anti-inflammatory, C-reactive protein, Statins

INTRODUCTION

Dyslipidemia is a quantitative or qualitative abnormality in plasma lipid. It is a modifiable cardiovascular disease (CVD) risk factor. The other major CVD risk factors associated with dyslipidemia are hypertension, diabetes mellitus, obesity and smoking.[1] NCEP/ATP III has recommended an intensive management of dyslipidemia to decline the burden of cardiovascular death. The management of dyslipidemia includes non-pharmacological and pharmacological measures.

Non pharmacological management involves dietary advice and aerobic exercise, reported to control the body weight and visceral fat of dyslipidemic patients leading to an acceptable reduction in serum lipid level.[1] However, there are patients who require medications to improve their outcome.

Statins, which are analogs of 3-Hydroxy-3-methylglutaryl co-enzyme A (HMG-COA) and inhibitors of the rate limiting step of cholesterol synthesis are the most commonly prescribed cholesterol lowering drugs world-wide.[2] Statins also have non-cholesterol lowering effects known as pleiotropic effects. Anti-inflammatory properties are one of these pleiotropic effects of statins. Certain inflammatory molecules have been implicated in artherosclerotic processes, including pro-inflammatory cytokines (e.g. Interleukin-1, tumor necrosis factor-α), adhesion molecules (e.g. intercellular adhesion molecule-1, selectins), products of hepatic stimulation like C-reactive protein and other acute phase reactants.[3] The best

validated inflammatory marker in artherosclerosis is C-reactive protein.

METHODS

Description of study area

The study was carried out in the University of Port-Harcourt Teaching Hospital (UPTH), Port-Harcourt, which is a main referral center for Rivers State.

Study population

The subjects included all patients presenting with dyslipidemia, who were about to be commenced on statins. Dyslipidemic patients who have similar illnesses but have not been commenced on statins were recruited as control subjects. Dyslipidemia was defined as total cholesterol ≥5.17mmol/l (200mg/dl), LDL-C ≥3.36mmol/l (130mg/dl), high density lipoprotein cholesterol (HDL-C) ≤1.03mmol/l (40mg/dl) for males, ≤1.3mmol/l (50mg/dl) for females and Serum TG ≥1.7mmmol/l (150mg/dl) using ATP III criteria.

Inclusion criteria

- Dyslipidemic diabetic, hypertensives, stroke and obese who were about to be commenced on statins
- Aged 18years and above and have given an informed written consent.

Exclusion criteria

- Dyslipidemic patients who have not given an informed written consent
- Patients have evidence of sepsis
- Autoimmune disorders or other inflammatory condition
- Patients who are also on anti-inflammatory drugs like corticosteroids or Non-steroidal anti-inflammatory drugs
- Pregnant with positive B-HCG test or too ill.

Inclusion criteria

Age and sex matched patients who have given informed written consent but have not been commenced on statins.

Exclusion criteria

Patients who were unwilling to give an informed written consent or pregnant were excluded.

Ethical approval was obtained from the Research Ethics Committee of the University of Port Harcourt Teaching Hospital and University of Port-Harcourt before commencement of the study.

Subjects were recruited into the study using a systematic sampling technique. After adjusting for 10% attrition, calculated sample size was 160 for test subjects. 160 patients who have dyslipidemia but have not been commenced on statins were recruited as control. Total sample size was 320 subjects.

Study design

The study was a cohort study carried out over a period of 9 months from June 2017 to February 2018, where patients who have met the study criteria were recruited as test subjects. They had baseline highly sensitive quantitative C- reactive protein (HS-CRP) estimated using enzyme immunoassay, whose principle is based on latex agglutination. The normal value for Hs-CRP is less than 3mg/dl. Patients who had dyslipidemia but had not been commenced on statins were recruited as control subjects and both sets of subjects were followed-up and the above mentioned test repeated at 3 months.

Statistical analysis

Statistical Package for Social Sciences 22 (SPSS-22) was used for data analysis. Results were presented as mean±standard deviation for continuous variables. Continuous variables were compared with the students T-test, while proportions or categorical parameters were compared with chi-square test. A p value of less than 0.05 was considered statistically significant.

RESULTS

Total 366 patients were recruited, and 46 subjects were lost to follow-up. 320 subjects comprising of 160 test and 160 control subjects who met the study criteria were recruited and followed up over a period of 3 months.

Socio-demographic characteristics of the study population

The mean age±SD of the test subjects was 57.02±12.45 and that of the control was 51.86±13.27. Among the test subjects, 61.25% were females while 38.75% were males, however, 58.75% of the recruited control subjects were females compared to 41.25% who were males.

Majority of the test subjects, 54.38% and control subjects, 58.75% had tertiary education, 20.63% of the test subjects had secondary education compared to 8.75% of the control subject. 17.50% of both the test and control subjects had their highest educational qualification as primary, while 7.5% of the test subjects had no education compared to 15% of the control subjects.

Majority of the test subjects were married (81.3%), 6.25% were single, 3.75% were divorced, while 8.75% were widowed. 82.50% of the control subjects were married, 17.5% were widowed, none of the control subject was single or divorced (Table 1).

Table 1: Socio-demographic characteristics of the study population.

Socio-demographics	Test subjects (N=160) Freq (%)	Control (N=160) Freq (%)	Total (N=320) Freq (%)
Age (Mean±SD)	57.02 ±12.45	51.86±13.27	
Age group			
21-30	0 (0.00)	24 (15.00)	24 (7.50)
31-40	22 (13.75)	22 (13.75)	44 (13.75)
41-50	17 (10.63)	16 (10.00)	33 (10.31)
51-60	58 (36.25)	42 (26.25)	100 (31.25)
61-70	43 (26.88)	56 (35.00)	99 (30.94)
>70	20 (12.50)	0 (0.00)	20 (6.25)
Sex			
Female	98 (61.25)	94 (58.75)	192 (60.0)
Male	62 (38.75)	66 (41.25)	128 (40.0)
Educational level			
No formal education	12 (7.50)	24 (15.00)	36 (11.25)
Primary	28 (17.50)	28 (17.50)	56 (17.50)
Secondary	33 (20.63)	14 (8.75)	4 7(14.69)
Tertiary	87 (54.38)	94 (58.75)	181 (56.56)
Marital status			
Single	10 (6.25)	0 (0.00)	10 (3.13)
Married	130 (81.25)	132 (82.50)	262 (81.88)
Divorced	6 (3.75)	0 (0.00)	6 (1.88)
Widowed	14 (8.75)	28 (17.5)	42 (13.13)

Pattern of medical illnesses of the study subjects

Among the test subjects, 102 (63.7%) were hypertensives, 97 (60.6%) were diabetics and 14 (8.8%) had stroke.

Among the control subjects, 92 (57.5%) had hypertension, 70 (47.5%) had diabetes, while 4 (2.5%) had stroke. Some of the test and control subjects had more than one medical illness as shown in Figure 1.

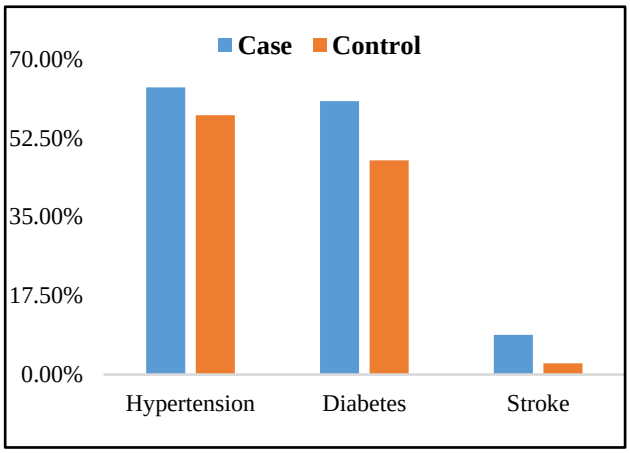

Figure 1: Medical conditions of the study subjects.

Pattern of dyslipidemia among the subjects

Among the test subjects, the commonest form of dyslipidemia was high total cholesterol reported by 85 (53.1%) of the recruited subjects, 84 (52.5%) of the test subjects had high LDL-Cholesterol, 68 (42.5%) had low HDL-Cholesterol, and hypertriglyceridemia 44 (27.5%) was the least pattern of dyslipidemia among the test subjects.

Among the 160 recruited control subjects, high LDL-Cholesterol was the most prevalent pattern of dyslipidemia seen in 94 (58.7%) of the control, 80 (50%) had high total cholesterol as well as hypertriglyceridemia, and the least pattern of dyslipidemia was low-HDL cholesterol found in 42 (26.2%) of the control subjects as shown in Figure 2.

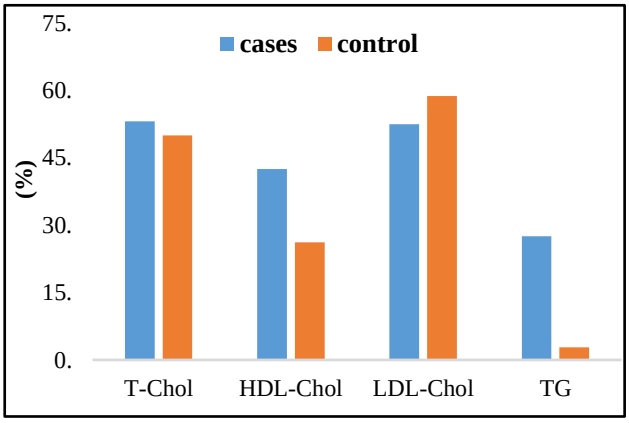

Figure 2: Pattern of dyslipidemia among the test subjects and control.

There was also no significant relationship between doses of statin and c-reactive protein as shown in Table 2.

Table 2: Association between the doses of statin and changes C-reactive protein of the test subjects using Pearson's correlational coefficient(r).

Variables	r	95% CI	p-value
CRP	0.096	-0.118, 0.492	0.227

Table 3 shows that the mean CRP of the test subjects on commencement of statin was 11.14±7.19, but subsequently reduced significantly by 3.98±4.9 after 3months of therapy.

The mean CRP of the control subjects was 11.98±3.33 and subsequently reduced by 1.81±3.4 three months later. The reduction in the CRP of the control subjects was not statistically significant. As shown in Table 4, patients who were on both statins had a significant reduction of their C-reactive proteins, however, the mean reduction in C-reactive protein was higher for artovastatin treated patients when compared to rosuvastatin (4.86 vs 3.65) after 3 months of therapy.

Table 3: Comparison of the mean C-reactive protein of the test and control subjects at the start and after 3 months of statins therapy.

Inflammatory markers	Baseline (mean±SD)	3 months (mean±SD)	Mean±SD (decrease-) or (increase+)	Paired t test	p-value
CRP (mg/dl)					
Case	11.14±7.19	7.16±3.29	-3.98±4.9	10.20	0.001*
Control	11.98±3.33	10.33±3.5	-1.81±3.4	6.20	0.06

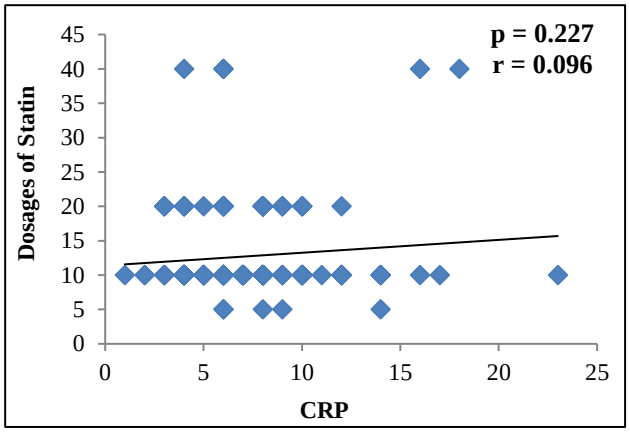

Figure 3: A scattered plot showing the Pearson's correlational coefficient between dosages of Statins and C-reactive protein.

Table 4: Comparison of the difference in the mean c-reactive protein of test subjects on artovastatin and rosuvastatin.

CRP(mg/dl)	Mean ±SD	Mean decrease	Paired t test	P-value
Rosuvastatin				
Start	10.63±5.6	3.65	9.63	0.01
3 months	6.97±2.8			
Artovastatin				
Start	12.51±10.3	4.86	4.47	0.01

DISCUSSION

Socio-demographics characteristics of the study population

More females were recruited into this study than males. This could be due to the health seeking behavior of females.

It could also be that the prevalence of dyslipidemia is higher among females when compared to males. This finding is consistent with a Chinese study where a higher prevalence of dyslipidemia was reported among females when compared to males.[5]

The mean age of the test subjects was 57.02±12.45, while that of the control subjects was 51.86±13.27. This is similar to the mean age of 55.15±16.12 reported in a Senegalese study.[6]

Pattern of dyslipidemia among the recruited subjects

High total cholesterol was the commonest form of dyslipidemia among the recruited test subjects with a prevalence of 53.1%, this is similar to the prevalence of 55.2% reported among type 2 diabetics presenting to the LUTH.[7] Also, in Edo state, high total cholesterol was also reported to be the commonest pattern of dyslipidemia among apparently healthy adults.[8] However, this wasn't consistent with the findings in a study done in Asaba, Nigeria, where low HDL-Cholesterol was found to be the most frequent form of dyslipidemia (60%) among apparently healthy professionals while the prevalence of high total cholesterol was 23%.[9] The inconsistency, could be as a result of the difference in the population of the participants recruited in both studies.

Effects of statins on C -reactive protein of test subjects

Patients who were on statins had a significant reduction in C-reactive protein when compared to those who were not on statins but there was a poor correlation between serum C-reactive protein and dosage of statins. The decline in mean C-reactive protein of the test subjects on artovastatin was more than rosuvastatin. This suggests that statins have anti-inflammatory effects in dyslipidemia and that artovastatin reduces C-reactive proteins more than rosuvastatin. This finding is similar to the report from a land mark U.S study, where artovastatin at 80mg and pravastatin (40mg) were reported to significantly reduce C-reactive protein after 30 days of statin therapy, and in that study, patients who had more than 2mg/l decrease in C-reactive protein had better clinical outcome irrespective of LDL-cholesterol levels.[10]

CONCLUSION

Statins significantly reduced C-reactive protein concentration of dyslipidemic patient. However, there was no significant correlation between the dose of statins and its effects on C-reactive protein.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Research Ethics Committee of the University

of Port Harcourt Teaching Hospital and University of Port-Harcourt

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Cite this article as: Egboh SC, Iyeopu MS. Effects of statins on the c-reactive protein of dyslipidemic patients in the university of Port-Harcourt teaching hospital. Int J Res Med Sci 2018;6:3259-63.