ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 7, Issue 3, 2014

ISSN - 0974-2441

Original Article

DYSLIPIDEMIC FEMALES HAVE EQUAL RISK TO CARDIAC DISEASES AS MALES - A NEUTROPHIL MEDIATED PATHWAY.

N.KARTHICK[1], K.N.POORNIMA[1], K.DILARA[2], G.THILIP KUMAR[1], A.SARAVANAN[3]

1. Tutor, Department of Physiology, SRM Medical college Hospital & Research centre, Kattankulathur, 2. Professor, Department of Physiology, Sri Ramachandra Medical College & Research institute, Porur., 3. Professor and Head, Department of Physiology, SRM Medical college Hospital & Research centre, Kattankulathur,

E mail id: karthicpoornima@gmail.com, karthick.nedu@gmail.com

Received: 3 May 2014, Revised and Accepted: 30 May 2014

ABSTRACT

Objective: Coronary artery disease (CAD) is one of the leading cause of death in adult women. Dyslipidemia is one of the major risk factor for CAD and it further causes proliferation of neutrophils and monocytes. Neutrophil is the hall mark for inflammation and involve in the development of early atherogenesis. The objective of the current study is to evaluate the effect of dyslipidemia on neutrophil count in dyslipidemic male and female.

Methods: The study group included 49 patients with dyslipidemia and 49 age and sex matched healthy controls. The lipid profile and various hematological parameters were estimated.

Result: Total leucocyte and neutrophil count is significantly increased in dyslipidemic patients and there is no significant difference between male and female dyslipidemic subjects, both are equally affected.

Conclusion: The study concludes that rise in neutrophil count in dyslipidemic subjects is an additional risk for early atherosclerotic lesions and coronary artery disease.

Keywords: Dyslipidemia, Neutrophil, Coronary artery disease (CAD)

INTRODUCTION

Coronary artery disease (CAD) is the leading cause of death and disability among adult women accounting for deaths of 1in 3 women [1].1 in 9 women is diagnosed with some form of cardiovascular diseases between the age group of 45-64 [2]. According to WHO, by 2013 it is expected that 23 million people will die for cardiovascular disorders annually, women being the maximum victims. A premenopausal woman who has a heart attack has twice the death rate of a similarly aged man. The association of smoking, hypertension, dyslipidemia and diabetes with CAD is well established. Dyslipidemia, one of the prime risk factor for CAD, induces neutrophilia by promoting proliferation, mobilization and differentiation of Haemopoietic stem/progenitor cell (HSPC) and thereby increasing granulocytes and monocytes [3]. Increase in neutrophil and monocyte recruitment promotes early atherogenesis in the vessels and increases the risk of CAD in dyslipidemic individual. The excess CAD mortality among Asian Indians is greater in women than in men [4]. Traditionally epidemiological studies of CAD have been focused more on men therefore the present study aims to determine the effect of dyslipidemia on neutrophil count in both male and female dyslipidemic individuals.

MATERIALS AND METHODS

49 subjects with dyslipidemia defined by elevation of plasma cholesterol, triglycerides (TGs) or both, or a low high density lipoprotein level and 49 healthy age and sex matched subjects voluntarily attending our master health checkup clinic were enrolled in this study. Both control and dyslipidemia group contains 20 females and 29 males each.

All participants including dyslipidemia and controls gave a written informed consent to participate in this study. Patients with H/O respiratory diseases, cardiovascular diseases, hypertension, and diabetes mellitus were excluded from the study.

Handling and storing of blood samples was done as per criteria furnished by national committee for clinical laboratory standard (NCCLS). Blood was collected after 12 hours fasting, in the morning between 8 – 9 am. Blood samples were collected in two tubes by observing universal precaution for venipuncture. To the first tube 2ml of blood was transferred and the blood was allowed to clot for serum separation. Serum was separated and stored at -70c until assay. SIEMENS kit was used for the analysis lipid profile. The second tube containing the anti-coagulant EDTA, 5ml of blood was added to that tube for the analysis of hematological parameters such as RBC, total and differential count of WBC, Hb, PCV and platelets and they are estimated by automatic cell counter. The study was approved by the institutional ethical committee.

Data are presented as the mean ± SD. Statistical analysis was performed by an IBM computer with the use of statistical package of social science (SPSS) ver. 21.0. Independent t test was used to showing differences between dyslipidemia group and controls. The level of significance was set at $p < 0.05$.

RESULTS

Table 1 shows the comparisons of lipid parameter between the dyslipidemic subjects and the control subjects. The cholesterol, Low density lipoprotein (LDL) and cholesterol – High density lipoprotein ratio were significantly higher in group 1 when compared to group 2, hence group 1 called as dyslipidemic subjects and group 2 called as control subjects. The Triglyceride and High density lipoprotein (HDL) did not show any significant difference.

Table 2 shows the comparisons of Neutrophil between the dyslipidemic and the control group. Neutrophil were significantly higher in group 1 when compared to group 2.

Table 1: Independent t-Test- Comparisons of Lipid parameter between group 1 and group 2

Parameter	**Dyslipidemic (Group1)** (n=49) Mean ± SD	**Control (Group2)** (n=49) Mean ± SD	t-value	p-value
CHOLESTROL	225.63 ± 32.082	168.45 ± 22.021	10.287	.000
TRIGLYCERIDE	137.45 ± 64.747	127.92 ± 76.860	.664	.508
HDL	45.37 ± 10.315	41.63 ± 7.265	2.072	.41
LDL	155.18 ± 28.658	101.51 ± 19.131	10.904	.000
CHO_HDL_RATIO	5.0959 ± 1.18878	4.1694 ±.81909	4.493	.000

Data were expressed as Mean ± SD. P value <0.05 was considered as significant. (*p=<0.05, **p=<0.001)

Table 2: Independent t-Test- Comparisons of Neutrophil between group 1 and group 2

Parameter	Dyslipidemic (Group1) (n=49) Mean ± SD	Control (Group2) (n=49) Mean ± SD	t-value	p-value
Neutrophil	68.03 ± 4.359	54.00 ± 5.303	14.312	.000

Data were expressed as Mean ± SD. P value <0.05 was considered as significant. (*p=<0.05, **p=<0.001)

Table 3 shows the comparisons of Neutrophil between the male dyslipidemic and female dyslipidemic subjects. There was no significant difference observed between male and female dyslipidemic subjects.

Table 3: Independent t-Test- Comparisons of Neutrophil between Male and Female Dyslipidemic subjects

Parameter	Dyslipidemic Male (n=29) Mean ± SD	Dyslipidemic Female (n=20) Mean ± SD	t-value	p-value
Neutrophil	67.79 ± 4.800	68.38 ± 3.717	-.462	.646

Data were expressed as Mean ± SD. P value <0.05 was considered as significant. (*p=<0.05, **p=<0.001)

DISCUSSION

Dyslipidemia is elevation of plasma cholesterol, triglycerides (TGs) or both or a low HDL that contributes to the development of atherosclerosis. Dyslipidemia may be one of the first clues to the diagnosis of various diseases including CAD, subclinical hypothyroidism etc… [5, 6] often dyslipidemia is found to be associated with neutrophilia [7]. Increase in LDL, Cholesterol or triglycerides causes HSPC differentiation toward atherogenic monocytes and neutrophil [1, 8]. In our study we found that there is positive correlation between lipid levels and neutrophil count. As the lipid level increases there is increase in neutrophils. Dyslipidemia combined with neutrophilia impose a greater risk on cardiovascular system as neutrophilia is found to be associated with early atherogenesis and histopathologic features of rupture prone lesions [9]. The underlying pathogenesis of CAD is characterized by chronic inflammation due to both loss of endothelial integrity and sub endothelial retention of LDL [10]. The mechanism of atherosclerosis in neutrophilia is mainly due to granules secreted and released from neutrophil which causes loss in integrity of endothelium. Myeloperoxidase, the most abundant protein in neutrophils is associated with increased risk of cardiac events [11]. Human neutrophil peptides are markedly increased in acute coronary diseases. HNPs form complexes with LDL and increases LDL binding to the endothelial surface which leads to endothelial dysfunction [12]. Other neutrophil specific proteases which link to matrix degradation such as elastase, metalloproteinase are found to be correlated with adverse cardiac events [13]. Furthermore these granule proteins have shown to play a role in recruitment of inflammatory monocytes [14]. Studies have shown that neutropenic mice display reduced plaque sizes at early stage. In our study we have found that there is no significant difference found in neutrophil count between male and female dyslipidemic subjects. Hence dyslipidemic females have equal risk to cardiac diseases as male. So, this proves that dyslipidemia mediated neutrophilia is an additional risk factor for CAD.

CONCLUSION

Coronary artery disease in women continues to be a major risk for the mortality and morbidity of women. Abnormality of Cholesterol metabolism may lead to cardiovascular disease and heart attacks [15]. Women have a higher frequency of angina than man. Young women with obstructive CAD experience a significantly worse outcome when compared with men of same age [16]. The risk of CAD is associated with many factors such as obesity, family history, diabetes, dyslipidemia, hypertension, etc., our study suggests that the neutrophilia should be viewed as an independent risk factor for CAD in dyslipidemic individuals. Improved understanding of gender differences in clinical presentations symptoms, treatment and outcome of CAD is needed. Future studies can be done to find out the possible therapeutic intervention to block the mechanism of dyslipidemia in proliferation of HSPCs.

REFERENCES

1. Dallas, Tex : American Heart Association. Heart and stroke statistical update 2001.
2. Agrawal M, Gupta M, Gupta A, Agrawal A, Sarkari A, Lavania P. Prospective randomized trial comparing efficacy of alfuzosin and tamsulosin in management of lower ureteral stones. Urology 2009;73(4):706-9.
3. Avinash MB, Subrahmanyam KS, Sundarayya Y, Govindaraju T. Covalent modification and exfoliation of graphene oxide using ferrocene. Nanoscale 2010;2(9):1762-6.
4. Baigent C, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C, et al. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. Lancet 2005;366(9493):1267-78.
5. Baldus S, Heeschen C, Meinertz T, Zeiher AM, Eiserich JP, Simoons ML, et al. Münzel T, Myeloperoxidase serum levels predict risk in patients with acute coronary syndromes. Circulation 108 12 12 Slutsky As Human neutrophil peptides A novel potential mediator of inflammatory cardiovascular diseases Am Heart Circ Physiol Nov 2008;295(5):1440-5.
6. Biren N, Khodidas D. Shah, Raiyani and D. C ModiAntiurolithiatic Activity Studies of MomordicacharantiaLinn Fruits International Journal of Pharmacy Research and Technology 2011;1(1):06-11.
7. Ebenezer P, Akila S, J. Renuka Prevalence of Metabolic Syndrome and Its Components in Women with Subclinical Hypothyroidism Asian Clin Res. vol 2013;6(4):82-4.
8. Enas EA, Senthilkumar A, Juturu V, Gupta R. Coronary artery disease in women. Indian Heart J 2001;53(3):282-92.
9. Ionita MG, van den Borne P, Catanzariti LM, Moll FL, de Vries J-PPM, Pasterkamp G, et al. High neutrophil numbers in human carotid atherosclerotic plaques are associated with characteristics of rupture-prone lesions. Arterioscler Thromb Vasc Biol 2010;30(9):1842-8.

10. Karthick N, Dillara K, Poornima KN, Subhasini AS. Dyslipidaemic changes in women with subclinical hypothyroidism. Journal of clinical and diagnostic research : JCDR 2013;7(10):2122-5.
11. Leclercq A, Houard X, Philippe M, Ollivier V, Sebbag U, Meilhac O, et al. Involvement of intraplaque hemorrhage in atherothrombosis evolution via neutrophil protease enrichment. J Leukoc Biol 2007;82(6):1420-9.
12. Reddy A, Meera S, Kumar JS. Sreenivas Ebenezer William, Correlation between glycemic control and lipid profile in type 2 diabetic patients: hba1c as an indirect indicator of dyslipidemia. Asian j pharm clin res vol 7 issue2;2014:153-5.
13. Skalen K, Gustafsson M, Rydberg EK, Hulten LM, Wiklund O. Subendothelial retention of atherogenic lipoproteins in early atherosclerosis. Nature 2002;417:750-4.
14. Soehnlein O, Lindbom L, Weber C. Mechanisms underlying neutrophil-mediated monocyte recruitment. Blood 2009;114(21):4613-23.
15. Thom T, Hasse N, Rosamond W. et al: Heart disease and stroke statistics- update: A report from the American Heart Association statistics committee and stroke statistics subcommittee. Circulation e85 2006;113.
16. Tolani S, Pagler TA, Murphy AJ, Bochem AE, Abramowicz S, Welch C, et al. Hypercholesterolemia and reduced HDL-C promote hematopoietic stem cell proliferation and monocytosis: studies in mice and FH children. Atherosclerosis 2013;229(1):79-85.