

ORIGINAL ARTICLE

Effects of Vitamin E in the Management of Dyslipidemia in Combination with Statin Therapy

MUHAMMAD ISHAQUE BHATTI¹, RAZIA BANO², FAZEELA RIZWAN MEMON³, MADIHA SHAH², RIZWAN AHMED MEMON⁴, ALI RAZA MEMON¹

¹Post Graduate Candidate; Department of Biochemistry; Liaquat University of Medical & Health Sciences Jamshoro, (LUMHS) Sindh

²Assistant Professor; Medical Unit-II, Department of Medicine, Liaquat University of Medical & Health Sciences (LUMHS) Jamshoro, Sindh

³Lecturer, Department of Pharmacology, Shaheed Mohtarma Benazir Bhutto Medical University of Medical & Health Sciences Larkana.

⁴Assistant Professor. Medical Unit-II, Department of Medicine, Liaquat University of Medical & Health Sciences (LUMHS) Jamshoro, Sindh

⁵Lecturer, Department of Pharmacology, Liaquat University of Medical & Health Sciences Jamshoro, (LUMHS).

⁶Assistant Professor ; Department of Biochemistry, Liaquat University of Medical & Health Sciences Jamshoro, (LUMHS)

Correspondence to Dr. Ali Raza Memon, Email: ali.bio.lumhs@gmail.com

ABSTRACT

Aim: To determine the effects of vitamin E therapy in the management of dyslipidemia with combination of statin drugs and also to determine the efficacy of statin drugs with combination of vitamin E therapy.

Methodology: This case control study was conducted at LUMHS Jamshoro. Total 200 patients of dyslipidemia with the age between 30 to 50 years were included with mentioned inclusion and exclusion criteria & were divided in to two groups; control group who received only statin drugs for treatment of dyslipidemia and case control group who received statin drugs along with Vitamin E 800 mgs in divided dose. The fasting blood glucose level was measured by glucose oxidase method while lipid profile parameters serum cholesterol, TG's, Serum LDL levels were estimated byenzymic calorific method on Cobas auto analyzer (model c-111 ACN 435 GERMANY) while HbA1c% was estimated on microlab. The statistical analysis was done on SPSS version 21 by applying unpaired student t test and ANOVA. The p value less than 0.05 consider as significant.

Results: Finally after treatment phase the Mean & SD value of serum cholesterol in control group was 209.13 ± 5.15 mg/dl while in case study group was 189.51 ± 6.11 mg/dl, serum TG's levels in control group was 191.52 ± 7.83 mg/dl & case study group was 168.56 ± 7.81 mg/dl, serum LDL levels in control group was 120.44 ± 4.67 mg/dl & in case study group was 97.15 ± 5.76 mg/dl. All parameters of lipid profile significantly decline in case study group.

Conclusion: This research concluded that there is strong positive impact of vitamin E along with statin therapy on the management of dyslipidemia and in prevention of cardiovascular complications.

Keywords: Dyslipidemia, Vitamin E, Statin Drugs.

INTRODUCTION

Dyslipidemia is basically disruption of lipid profile in blood.¹ Hyperlipidemia also consider as dyslipidemia². Elevated level of serum cholesterol, triglycerides (TG's), low density lipoproteins (LDL) labeled as dyslipidemia³. Dyslipidemia is one of the leading causes of development of different cardiovascular complications like atherosclerosis, angina, myocardial infarction, type-2 diabetes mellitus, cerebral stroke etc^{4,5}. Dyslipidemia also consider as primary independent factor for the development of cardiovascular disorders (CVD) in Asian population.⁶ In the European developed countries the incidence CVD increasing associated with dyslipidemia.⁷ The more than 17% adult population of Pakistan has suffering from dyslipidemia which is alarming indication for future morbidity and mortality.⁸ The statin therapy commonly use all over the world for the management of dyslipidemia⁹. Vitamin E is one of the fat soluble, essential vitamin because it cannot synthesize inside the human body. It is natural antioxidant due to its antioxidant property it consider as cardio protective as well as hepatic protective agent^{10,11}. Vitamin E consider as cardio protective agent because it lowers the serum cholesterol level, LDL level as well.¹¹ The active component of vitamin E, alpha tocopherol and tocotrienol inhibiting the cholesterol synthesis by post-transcriptional suppression of regulatory enzyme of cholesterol metabolism i.e HMG CoA Reductase^{12,13}. Vitamin E also suppresses the lipid peroxidation process by inhibiting the protein kinase C and phospholipase A2.¹⁴ These possible mechanism can prevent the development of cardiovascular complications occur due to dyslipidemia.

The aim of this study to know the effects of vitamin E therapy in the management of dyslipidemia with combination of statin drugs and also to determine the efficacy of statin drugs with combination of vitamin E therapy.

METHODOLOGY

This case control study was conducted after approval from Ethical Committee, at Liaquat University of Medical & Health Sciences (LUMHS) Jamshoro from July 2021 to September 2021. Total 200 patients with dyslipidemia were selected from medical OPD LUMHS Hospital Hyderabad, Jamshoro. The sampling was done on Non Probability type of sample technique. The age between 30 to 50 years both male & females with disturb lipid profile serum cholesterol ranges from 220 to 250mg/dl, TG's levels ranges from 180 to 250mg/dl while LDL levels ranges between from 120 to 160mg/dl, with BMI up to 25, with or without history of hypertension, cases of initial or newly diagnosed cases of type-2 diabetes mellitus with HbA1c% under 8.5% without any major cardiac problem were included in this research while the patients with age less than 30 or more than 50 years, highly disturbed levels of lipid profile beyond the range mentioned at inclusion criteria, known old case of type-2 diabetes mellitus, myocardial infarction, history of Bypass cardiac surgery, liver disorders were excluded from this study. Total samples were divided in to two groups control group (A) contained 100 subjects who received only the statin drugs like tablet; Lipiget 10mg or Rovista 10mg once a day after dinner for treatment of dyslipidemia. While case study group (B) contained 100 cases of dyslipidemia they received statin drugs same group as in control group along with 800mg of vitamin E; capsule Evion 400mg two times a day for period of one month. 5 ml of blood with 10 -12 hours of fasting condition, sample was collected from each subjects at two levels first at level zero means before start of the research and second at level-I after completion of one month of therapy. After the centrifugation of blood sample samples were analyzed for different biochemical parameters. The fasting blood glucose level was measured by glucose oxidase method while lipid profile parameters serum cholesterol, TG's, Serum LDL levels were estimated byenzymic calorific method on Cobas auto analyzer (model c-111 ACN 435 GERMANY) while HbA1c% was estimated on microlab. The statistical analysis was

Received on 10-10-2021

Accepted on 09-02-2022

done on SPSS version 21 by applying unpaired student t test and ANOVA. The p value less than 0.05 consider as significant.

RESULTS

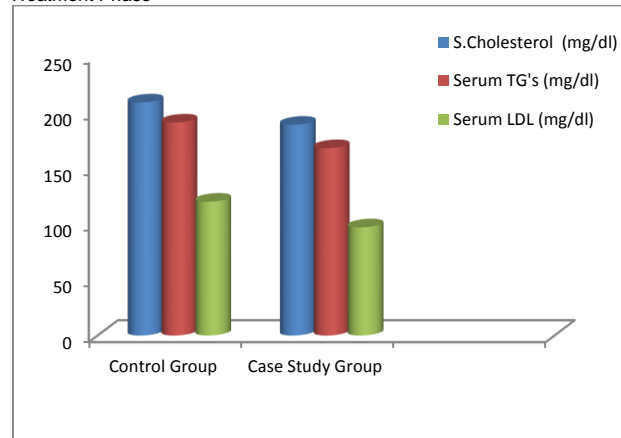
Total 200 subjects were participated in this research study the mean age with SD in control group was 41.2 ± 5.60 while in case study group it was 40.30 ± 4.58 . The mean BMI in control group was 21.13 ± 3.05 while in case study group it was 20.35 ± 3.82 . The mean fasting blood glucose levels in control group was 99.12 ± 6.11 mg/dl while in case study group it was 97.88 ± 6.35 mg/dl. The mean systolic blood pressure of control group was 117.11 ± 5.22 mmHg while in case study group it was 75.61 ± 7.32 mmHg. The mean HbA1c% of control group was 6.3 ± 0.48 % while in case study group it was 6.6 ± 1.37 %. This research contained 44 hypertensive & 49 diabetic subjects in control group while 47 hypertensive & 37 diabetic subjects in case study group. The lipid profile parameters under study serum cholesterol, serum TG's and serum LDL levels were mentioned in below table before and after treatment phase.

Table 1: Lipid Profile Parameters under Study in Control & Case Study Groups

The Mean & SD values Biochemical Parameters of Control Group (A) Before & After treatment Phase		
Parameters	At Zero Level	At level -I
Serum Cholesterol (mg/dl)	242.19 ± 5.33	209.13 ± 5.15 *
Serum TG (mg/dl)	232.71 ± 9.05	191.52 ± 7.83 *
Serum LDL (mg/dl)	148 ± 6.38	120.44 ± 4.67
The Mean & SD values Biochemical Parameters of Case Study Group (B) Before & After treatment Phase		
Serum Cholesterol (mg/dl)	239.09 ± 7.57	189.51 ± 6.11 **
Serum TG (mg/dl)	231.33 ± 6.15	168.56 ± 7.81 **
Serum LDL (mg/dl)	145.63 ± 9.26	97.15 ± 5.76 **

(* indicate p values < 0.05; ** p. value < 0.01)

Graph 1: Lipid Profile Parameters in Control & Case Study Group after Treatment Phase



The above results show that there was highly significant decline in lipid profile parameters in case study group who were used vitamin E along with statin therapy.

DISCUSSION

Dyslipidemia is one of the leading cause of morbidity & mortality all over the world because it can leads the development of cardiovascular complications^{4, 5} like initially development of atherosclerosis; it can deposit the cholesterol and TG's at major cardiac arteries by accumulation of the plasma lipoproteins in large arteries.¹⁵ Atherosclerosis basically it is chronic inflammation in which free reactive species (RS) has been formed by cellular damage and can lead to destruction of carbohydrates, lipids, proteins and nucleic acid components of cell.^{16, 17} After this event the lipid peroxidation and LDL oxidation is the initial and main step

in formation of lesions of the atherosclerosis¹⁸. Hypercholesterolemia is one of the leading cause of cardiovascular morbidity and mortality also because it develop the fibrous plaque due to lipid oxidation and LDL oxidation causes the endothelial damage and finally development of thrombus formation which lead cardiovascular complications like hypertension, angina, myocardial infarction and cardiac failure etc^{19,20}. The statin drugs like atorvastatin, ruvastatin etc are clinically use for the treatment of dyslipidemia but with statin drugs many patients complained with muscular cramps and G.I.T disturbances²¹.

Herbert Evans in 1922 from green leafy vegetables discovered the vitamin E²². Vitamin E has different isoforms like alpha, beta, gamma, sigma tocopherols but alpha tocopherol consider as gold standard type of vitamin E with proper biological activities and natural anti oxidant properties²³. This alpha tocopherol inhibit the synthesis of cholesterol by inhibiting the rate limiting enzyme of cholesterol synthesis i.e., HMG CoA Reductase²⁴; statin drugs also inhibit this enzyme but vitamin E has one beauty also that it strong suppress the LDL oxidation which is highly beneficial in prevention for development of cardiovascular complications²⁵.

Our study strongly supported by Negis et al (2006),²⁶ Traber et al (2007),²⁷ they reported that administration of vitamin E reduce the serum cholesterol level also reduce the inflammation of arteries and damage of endothelial cells because intake of vitamin E in foods inhibit the oxidation of LDL & lipid peroxidation.

In our study there are some limitations that sample size only collected from one hospital which cover few cities of Sindh. In future there will be need of same study on large scale sample size and samples will collect from different main district hospitals of Sindh. Duration of study or treatment only one month, so needs to check the proper effects at least up to three to six months therapy. Our study also singly dose of vitamin i.e 800mgs/day but can study the effects of vitamin E according their different dosage like effects on 400 mgs/day, 800 mgs/day and 1200mgs/day.

CONCLUSION

This research concluded that there is strong positive impact of vitamin E along with statin therapy on the management of dyslipidemia and in prevention of cardiovascular complications. Vitamin E also increases the efficacy of statin drugs with its combination and reduce the complaints of muscular cramps as well from the patients.

Conflict of Interest: There is no any conflict of interest.

REFERENCES

1. Kwon J, Lee C, Heo S, Kim B, Hyun CK. DSS-induced colitis is associated with adipose tissue dysfunction and disrupted hepatic lipid metabolism leading to hepatosteatosis and dyslipidemia in mice. *Scientific reports*. 2021 Mar 5;11(1):1-6.
2. Tsao CF, Chang CM, Weng SW, Wang PW, Lin CY, Lu SN. Identifying endemic areas and estimating the prevalence of hyperlipidemia in Taiwan's townships. *Journal of the Formosan Medical Association*. 2021 Jan 1;120(1):460-5.
3. Wilms T, Boldrup L, Gu X, Coates PJ, Sgarbetta N, Nylander K. High Levels of Low-Density Lipoproteins Correlate with Improved Survival in Patients with Squamous Cell Carcinoma of the Head and Neck. *Biomedicines*. 2021 May;9(5):506.
4. Nguyen HD, Oh H, Kim MS. The association between curry-rice consumption and hypertension, type 2 diabetes, and depression: The findings from KNHANES 2012–2016. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*. 2021 Dec 26:102378.
5. Duc HN, Oh H, Yoon IM, Kim MS. Association between levels of thiamine intake, diabetes, cardiovascular diseases and depression in Korea: a national cross-sectional study. *Journal of nutritional science*. 2021;10.
6. Tam, C.H., Lim, C.K., Luk, A.O., Ng, A.C., Lee, H.M., Jiang, G., Lau, E.S., Fan, B., Wan, R., Kong, A.P. and Tam, W.H., 2021. Development of genome-wide polygenic risk scores for lipid traits and clinical applications for dyslipidemia, subclinical atherosclerosis, and diabetes cardiovascular complications among East Asians. *Genome medicine*, 13(1), pp.1-18.

7. Pirillo A, Casula M, Olmastroni E, Norata GD, Catapano AL. Global epidemiology of dyslipidaemias. *Nature Reviews Cardiology*.2021 Apr 8;1-2.
8. Shahid SU, Sarwar S. The abnormal lipid profile in obesity and coronary heart disease (CHD) in Pakistani subjects. *Lipids in health and disease*. 2020 Dec;19(1):1-7.
9. O'Malley, P.G., Arnold, M.J., Kelley, C., Spacek, L., Buelt, A., Natarajan, S., Donahue, M.P., Vagichev, E., Ballard-Hernandez, J., Logan, A. and Thomas, L., 2020. Management of dyslipidemia for cardiovascular disease risk reduction: synopsis of the 2020 updated US Department of Veterans Affairs and US Department of Defense clinical practice guideline. *Annals of internal medicine*, 173(10), pp.822-829.
10. O'Malley, P.G., Arnold, M.J., Kelley, C., Spacek, L., Buelt, A., Natarajan, S., Donahue, M.P., Vagichev, E., Ballard-Hernandez, J., Logan, A. and Thomas, L., 2020. Management of dyslipidemia for cardiovascular disease risk reduction: synopsis of the 2020 updated US Department of Veterans Affairs and US Department of Defense clinical practice guideline. *Annals of internal medicine*, 173(10), pp.822-829.
11. Al-Baiaty FD, Ismail A, Abdul Latiff Z, Muhammad Nawawi KN, Raja Ali RA, Mokhtar NM. Possible Hepatoprotective Effect of Tocotrienol-Rich Fraction Vitamin E in Non-alcoholic Fatty Liver Disease in Obese Children and Adolescents. *Frontiers in pediatrics*. 2021;9:675.
12. Abraham A, Kattoor AJ, Saldeen T, Mehta JL. Vitamin E and its anticancer effects. *Critical reviews in food science and nutrition*. 2019 Sep 25;59(17):2831-8.
13. Jiang Q. Natural forms of vitamin E and metabolites—regulation of cancer cell death and underlying mechanisms. *IUBMB life*. 2019 Apr;71(4):495-506.
14. Su LJ, Zhang JH, Gomez H, Murugan R, Hong X, Xu D, Jiang F, Peng ZY. Reactive oxygen species-induced lipid peroxidation in apoptosis, autophagy and ferroptosis. *Oxidative medicine and cellular longevity*. 2019 Oct 13;2019.
15. Rudel LL, Parks JS, Sawyer JK. Compared with dietary monounsaturated and saturated fat, polyunsaturated fat protects African green monkeys from coronary artery atherosclerosis. *Arteriosclerosis, thrombosis, and vascular biology*. 1995 Dec;15(12):2101-10.
16. Singh R, Devi S, Gollen R. Role of free radical in atherosclerosis, diabetes and dyslipidaemia: larger-than-life. *Diabetes / metabolism research and reviews*. 2015 Feb;31(2):113-26.
17. Ranneh Y, Ali F, Akim AM, Hamid HA, Khazaai H, Fadel A. Crosstalk between reactive oxygen species and pro-inflammatory markers in developing various chronic diseases: a review. *Applied Biological Chemistry*. 2017 Jun;60(3):327-38.
18. Rafeian-Kopaei M, Setorki M, Doudi M, Baradaran A, Nasri H. Atherosclerosis: process, indicators, risk factors and new hopes. *International journal of preventive medicine*. 2014 Aug;5(8):927.
19. Asada Y, Yamashita A, Sato Y, Hatakeyama K. Pathophysiology of atherothrombosis: Mechanisms of thrombus formation on disrupted atherosclerotic plaques. *Pathology international*. 2020 Jun;70(6):309-22.
20. Mageed L. Coronary artery disease: pathogenesis, progression of atherosclerosis and risk factors. *Open Journal of Cardiology & Heart Diseases*. 2018;2(4):1-7.
21. Thompson PD. The Clinical Presentation of Statin-Associated Muscle Symptoms (SAMS). In *Statin-Associated Muscle Symptoms 2020* (pp. 21-26). Springer, Cham.
22. Khalilouki F, Owen RW, Akdad M, El Bouhali B, Silvente-Poirot S, Poirot M. Vitamin E: an overview. *Molecular Nutrition*. 2020 Jan 1:51-66.
23. Hinman A, Holst CR, Latham JC, Bruegger JJ, Ulas G, McCusker KP, Amagata A, Davis D, Hoff KG, Kahn-Kirby AH, Kim V. Vitamin E hydroquinone is an endogenous regulator of ferroptosis via redox control of 15-lipoxygenase. *PLoS One*. 2018 Aug 15;13(8):e0201369.
24. Zingg JM. Vitamin E: regulatory role on signal transduction. *IUBMB life*. 2019 Apr;71(4):456-78.
25. Bhavnani BR, Cecutti A, Gerulath A, Woolever AC, Berco M. Comparison of the antioxidant effects of equine estrogens, red wine components, vitamin E, and probucol on low-density lipoprotein oxidation in postmenopausal women. *Menopause*. 2018 Nov 1;25(11):1214-23.
26. Negis Y, Aytan N, Ozer N, Ogru E, Libinaki R, Gianello R et al (2006) The effect of tocopheryl phosphates on atherosclerosis progression in rabbits fed with a high cholesterol diet. *Arch Biochem Biophys* 450(1):63–66.
27. Traber MG, Atkinson JM (2007) Vitamin E, antioxidant and nothing more. *Free Radic Biol Med* 43(1):4–15.