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Original Research Article.

Effects of Antioxidants (Vitamin C&E) on Blood Glucose, Serum Lipid Levels And Glycosylated Haemoglobin (HbA1c) in Diabetic, Hypertensive and Nutritional Anemic Patients

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ABSTRACT

Background: Diabetes & Hypertension are non-communicable diseases with vascular complications. Iron deficiency anemia is a major public health problem especially in developing countries. Combined effects of Vitamin C & E have beneficial effects on blood sugar post prandial, total cholesterol HbA1c, Systolic & Diastolic blood pressure. Both are used in treatment & prevention of anemia with improvement in various haematological responses accept haemoglobin.

Materials & Methods: A total of 420 cases were studied in Department of Physiology Santosh medical College I collaboration of Department of Medicine Sharda hospital. These patients were divided in 6 groups each of 70 per group. All 6 groups were further divided in Control & Test group 1, 2, 3. Control group comprises of diabetic, hypertensives & anemic patients already on treatments without supplementation of antioxidants & test group 1,2,3 were patients on treatments with supplementation of antioxidants. Pre supplementation their parameters were studied & after 12 weeks of supplementation of Vitamin C 500 mg given orally as Limcee tablet and Evion Vitamin E 400mg.

Results: Post prandial blood sugar levels, HbA1 c levels, both Systolic & Diastolic blood pressure & total cholesterol, all haematological investigations for anemia MCH, MCV, MCHC showed improvement except haemoglobin.

Keywords: Antioxidants, Diabetes, Hypertension, Anaemia.

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INTRODUCTION

Diabetes and hypertension are life style related non-Communicable disease, are of global significance. There is substantial overlap between their etiology and disease mechanism but the main factors in the etiology are genetic or environmental factors. Environmental factors include the period in utero, lifestyle factors as diet and physical activity. High intake of sodium, alcohol and unsaturated fat, smoking, lack of physical activity and mental stress are examples of an unhealthy lifestyle. Diabetes is due to the pancreas not producing enough insulin, or the beta cells of the body not responding efficiently to the insulin produced.[1] Statistically in 2018, an estimated 500 million people had diabetes worldwide[1], with type 2 diabetes making up almost 98% of the cases.[2,3] It is comprises of about 8.9% of the adult population[1], in both sexes.[4] Trends suggest that rates will continue to rise always annually.[1] Diabetes doubles a person's risk of early death. If someone has diabetes mellitus and hypertension, the ill effects in the body would be triple.

Anemias have reduction in circulating red-cell mass & hemoglobin below the normal level which is worldwide quite common. Circulating red blood cells (RBCs) have a protein known as haemoglobin, Iron is the major component of haemoglobin & it is the major carrier of oxygen. Decreased iron reserves in the body are important to produce hemoglobin, which stops the transport of oxygen to the organ systems of the body. Anemia reduces the oxygen-carrying capacity of the blood which in turn leads to tissue hypoxia which is described by hematocrit (the ratio of packed RBCs to blood volume) to the hemoglobin concentration.[5,6]

Antioxidants are exogenous which are supplemented orally as Vitamin C & Vitamin E & endogenous antioxidants as superoxide dismutase & adenosine both help together to neutralize free radicals.

Body's internal production of antioxidants is not enough to neutralize all the free radicals. We need our body to defend itself by increasing our dietary intake of antioxidant supplements which

help in blockade of generation of toxic metabolites and mediators. These include SOD, G-SH, carotene. Trace elements and minerals have antioxidant properties.

Antioxidant Supplements

Vitamin E, vitamin C and beta carotene. & trace elements that are components of antioxidant enzymes such as selenium, copper, zinc, and manganese.[7]

VITAMIN C (Ascorbic Acid)

Vitamin C is a water soluble vitamin and an important antioxidant, capable of scavenging or neutralizing cell damaging free radicals, because it acts as an electron donor.[8] The significance of Vitamin C in type2 diabetes mellitus has been suggested by the hypothesis that hyperglycaemia inhibits cellular uptake of dehydroascorbic acid (DHA), which is oxidized transportable form of Vitamin C.[9] In red cell, glucose strongly inhibits the uptake of DHA; therefore, hyperglycaemia in diabetes would be expected to cause vitamin C deficiency within the cell. DHA uptake into the cells is accomplished by glucose transporters, GLUT! & GLUT3, which transports DHA in competition to glucose[10], & this effect will be overcome by large intake of vitamin C.[11] Some studies show decrease in serum levels of vitamin C is due to decreased renal renal reabsorption of vitamin C & increased urinary excretion of vitamin C. Further studies have shown in diabetes there is a higher turnover of DHA to ascorbic acid is higher in diabetics. This higher turnover of vitamin C in diabetics underlie the need of higher dietary vitamin C requirements in diabetics Some studies show decrease in serum levels of vitamin C is due to decreased renal renal reabsorption of vitamin C & increased urinary excretion of vitamin C. Further studies have shown in diabetes there is a higher turnover of DHA to ascorbic acid is higher in diabetics. This higher turnover of vitamin C in diabetics underlie the need of higher dietary vitamin C requirements in diabetics. The biological mechanisms underlying lower vitamin C & E is by Inhibiting lipid peroxidation by antioxidants such as vitamin C. The mechanism of Vitamin E in Diabetes Mellites is it inhibits lipid peroxidation. An alternative method employs deuteration of polyunsaturated fatty acids (PUFA) at the methylene bridges (bis-allylic sites) between double bonds, which leads to the inhibition of the chain reaction courtesy of a kinetic isotope effect. Such D-PUFAs, for example, 11,11-D2-ethyl linoleate, suppress lipid peroxidation even at relatively low levels of incorporation into membranes. Two steps are involved in LIPID PEROXIDATION Initiation is the step in which a fatty acid radical is produced. The most notable initiators in living cells are reactive oxygen species (ROS), such as OH· and HOO·, which combines with a hydrogen atom to make water and a fatty acid radical & Propagation is when the fatty acid radical is not a very stable molecule, so it reacts readily with molecular oxygen, thereby creating a peroxyl fatty acid radical. This radical is also an unstable species that reacts with another free fatty acid, producing a different fatty acid radical and a lipid peroxide, or a cyclic peroxide if it had reacted with itself. This cycle continues, as the new fatty acid radical reacts in the same way.

The biological mechanisms underlying lower vitamin C levels in diabetics includes decreased cellular uptake, increased urinary loses, & increased metabolic turnover of Vitamin c in diabetes. These mechanisms suggest higher dietary intake of vitamin C requirements in diabetes, along with benefits of supplementation, as seen in type 3 diabetes. Vitamin E is a fat-soluble antioxidant as a supplement, Vitamin E has several health benefits for the body. Vitamin E is particularly important for the protection of our cell membranes as well as keeping our skin, heart and circulation, nerves, muscles, and red blood cells healthy. Vitamin E protect our cells against ill effects of dangerous free radicals, potentially damaging by-products of our body's metabolism. It can slow or stop the chain reactions caused by free radicals and therefore protect our cells from the harm of free radicals.[12]

MATERIALS & METHODS

It is a Interventional & Cross sectional or Longitudinal study. The study was conducted in the Department of Physiology, Santosh Medical College in collaboration with Department of Physiology & Department of Medicine, School of Medical Sciences and Research, Sharda Hospital, Greater Noida.

Patients attended medicine at Sharda Hospital, Greater Noida for treatment of anemia, diabetes and hypertension The study comprised of 420 patients further sub divided into 6 groups having three control groups and three test groups of diabetes, hypertension and anaemia respectively consisting 70 patients in each group with no family history anaemia, diabetes and hypertension. After taking full history and providing relevant information about the project and its implication voluntary participation was sought.

The patients were given Tablet Limcee (Vitamin C) of 500 mg and Tablet Evion (Vitamin E) of 400 mg as per requirement of study to each group of patients. All the supplements were given empty stomach daily once a day for 12 weeks. Patient were told to stop medication in case of adverse reactions like any allergic reaction etc & to investigate immediately.

General profile, relevant systemic examination of all systems & especially blood pressure was noted.

Clinical Parameters

Venous blood sample (as per requirement) was collected with complete aseptic precautions for blood counts, Plasma Glucose Levels, Glycosylated Hemoglobin and Lipid Profile.

Haematological & Biochemical parameters like Plasma Glucose Levels, Glycosylated Hemoglobin and Lipid Profile, complete blood counts (Haemoglobin, Total leucocyte count, Differential count, Platelet count, MCV, MCH, MCHC) were done by haematology cell counter (SYSMEX, XP100 cell counter).

- Glycosylated Haemoglobin-was done by BIORAD, D-10 analyser.
- Biochemical Assays on TRANSASIA, ERBA CHEM 5 PLUS analyser
- Plasma Glucose levels-were done by Glucose-Oxidase Method in the biochemistry lab.
- Serum Lipid levels- were measured using biochemistry auto analyser.
- Serum Cholesterol-By using enzymatic (cholesterol esterase) method.
- Triglycerides-By using enzygmatic (lipoprotein lipase) method.
- HDL Cholesterol-were measured by precipitation with phosphotungstate method/ Mg2+ method and cholesterol in supernatant was determined as per serum – cholesterol.
- VLDL-was calculated as Triglycerides/5
- LDL-calculated by Friedwaid formula: total cholesterol (HDLC +VLDL-C) Lipoprotein.

CUT OFF VALUES

- Fasting blood sugar-70-100mg/dl
- Post prandial blood sugar-100-120mg/dl
- Total Cholesterol-180-200mg/dl
- LDL-Cholesterol-60-129mg/dl
- HDl-Cholesterol-40-59mg/dl
- Serum Triglyceride-150-199mg/dl
- VLDL-2-30mg/dl
- MCV-80-100fl
- MCH-27-31pg
- MCHC-33.4%-33.5%

Statistical Evaluation

Data analysis was done as follows:

1. Mean values for age, height and weight in males and females were calculated and any variation was recorded.
2. Variation in the levels of glycosylated haemoglobin, blood glucose, parameters of lipid profile and haemoglobin of the diabetic/hypertensive/anaemic subjects in the age group of 18-60 years were studied and compared with the control group.
3. All the values were analysed statistically based on 'P' values.

Data Collection: The data was gathered in two phases i.e – pre supplementation and post supplementation.

In Pre-Supplementation Phase

After a preliminary discussion with the patient regarding the study, all the data was recorded, then supplementation was recommended to each patient in the experimental groups in the presence of physician along with the prescribed treatment.

- Dose and method of consuming the supplementation of antioxidants (vitamin C& E) were explained briefly to the patients.
- The patients were asked to revisit the clinic/OPD after six weeks.
- Telephone contacts during the supplementation phase was made to ensure the regular intake of supplementation in prescribed format.

In Post Supplementation Phase

After six weeks patients were asked to revisit the OPD/Clinic and repeat their haematological parameters (CBC & ESR), glycosylated haemoglobin, biochemical (lipid and sugar) estimation and some cardiovascular parameters (BP and pulse rate).

The collected data was analyzed by using IBM-SPSS version 22.0.

A written informed consent was taken from the patients.

Table 1: Comparison of blood sugar & HbA1clevels in diabetic patients of control group1 with test group 1

	Control group 1 with treatment without supplementation (1st reading) Mean ± SD	Test group on treatment without supplementation (2nd reading after 3 months) Mean ± SD	p value (p value <0.05 is statistically significant)
Fasting Blood Sugar level (mg/dl)	147.0± 17.02	145.8±18.42	0.68
Post Prandial Blood Sugar level (mg/dl)	265.05±38.33	299.9±36.6	<0.01*
HbA1c(%)	7.65±0.43	7.37±0.45	<0.01*

Table 2: Comparison of Blood Pressure (SBP & DBP) Control group 2 and Test Group 2 values in Hypertensive subjects.

Test	Control Group 2 on treatment without supplementation (1st reading) Mean± SD	Test Group 2 On treatment with supplementation (2nd reading after 3 months) Mean ± SD	p value (p value <0.05* is statistically significant)
Systolic Blood Pressure (mmhg)	161.48±10.85	165.67 ±11.43	0.027*
Diastolic Blood pressure (mmhg)	97.32± 10.61	92.82 ±9.25	<0.01*

Table 3: Comparison of lipid profile improvement in control group 2& test group 2

Lipid profile parameters	Control group 2 With treatment without supplementation (1st reading) Mean ± SD	Test group 2 on treatment with supplementation (2nd reading after 3 months) Mean ± SD	p value (p value <0.05* or equal to 0.05* is statistically significant)
Total cholesterol (mg/dl)	162.47 ±10.95	168.47 ±9.85	<0.01*
Triglycerides (mg/dl)	137.88±9.20	140.86±9.36	0.05*
HDL (mg/dl)	32.35±3.80	37.83 ±3.74	<0.01*
LDL (mg/dl)	109.45± 8.12	118.63±8.83	<0.01*
VLDL (mg/dl)	33.18±3.45	32.29±3.16	0.11*

Table 4: Comparison of complete blood counts parameters in anemic patients of control group 3 with test group 3

	Control group 3 with treatment Mean ± SD	Test group 3 post supplementation Mean ± SD	p value <0.05* is statistically significant
Haemoglobin	9.43 ±1.98	10.46 ±1.69	0.01*
PCV (%)	28.98±3.11	25.97 ±4.35	<0.01*
MCV (fl)	73.96 ±9.19	75.46 ±9.19	0.03*
MCH (pg)	23.75± 3.02	26.35 ±4.02	<0.01*
MCHC (gms %)	32.6 ±3.25	34.7± 4.25	0.01*
RBC Count (million/uL)	4.01 ±0.41	3.46± 1.28	<0.01

OBSERVATION AND RESULTS

In this study on comparison of control & test group 1 shows the mean ± SD of fasting blood sugar having statistically no significant change, the post prandial sugar and HbA1c in pre & post supplementation in control & test group 1 shows statistically significant difference ($p<0.05$))on comparison after 12 weeks statistically.[Table 1], on comparison showed after 12 weeks statistically significant changes in SBP & DBP of hypertensive control group 2 & test group 2 with significant p value.[Table 2]

In table Table 3 it shows all values statistically significant changes in lipid levels cholesterol in group2 &test group 2 and in Table 4 pre & post supplementation in test group 3 there were statistically insignificant change in complete blood count values with insignificant p value except haemoglobin & MCH which has significant changes with significant p value.

DISCUSSION

In Table 1 on comparison of control & test group 1 shows the mean ± SD of fasting blood sugar having statistically no significant change, the post prandial sugar and HbA1c in pre & post supplementation in control & test group 1 shows statistically significant difference ($p<0.05$) with 500mg of Limcee (vit C) & 400mg of Evion (vit E).On comparison in the study, Afkhami-Ardekani[13] proposed that, the previous clinical trials showed significant decrease in, FBS & HbA1c levels after usage of 1000mg/day of vitamin C or E separately in type 2 diabetics patients as Chen et al.[14] the daily consumption of 800mg of ascorbic acid for 4 weeks by type 2 diabetics patients caused no significant change in FBS 7 serum insulin due to use of lower doses. Forghani et al.[15] proposed significant decrease in HbA1c & LDL levels observed in patients supplemented with 1000mg/day of vitamin C FOR 6 weeks. Afkhami-Ardekani[13] showed significant decrease in total cholesterol was observed by using 2gm of vitamin C for 90 days.

Two steps are involved in Lipid Peroxidation Initiation is the step in which a fatty acid radical is produced. The most notable initiators in living cells are reactive oxygen species (ROS), such as $OH\cdot$ and $HOO\cdot$, which combines with a hydrogen atom to make water and a fatty acid radical & Propagation is when the fatty acid radical is not a very stable molecule, so it reacts readily with molecular oxygen, thereby creating a peroxyl fatty acid radical. This radical is also an unstable species that reacts with another free fatty acid, producing a different fatty acid radical and a lipid peroxide, or a cyclic peroxide if it had reacted with itself. This cycle continues, as the new fatty acid radical reacts in the same way Vitamin C & E both stop the chain reaction of initiation & propagation step in controlling blood fasting & post prandial levels of sugar Vitamin C in Hypertension is that it prevents cellular damage to proteins caused by oxidized lipids. As lipid peroxidation causes progression of atherosclerosis. Physiologic concentration of vitamin C inhibits it helps in reduction of blood pressure in vessels as it acts as a diuretic by reduces sodium and water retention so there no fluid retention, lowers blood pressure within blood vessels. Vitamin E in Hypertension halts the chain of lipid peoxidation.,eg it acts a chain breaking inhibitor of lipid perioxidation.[3] Both Vitamin E (alpha tocopherol), & vitamin C in Anemia are well Both Vitamin E (alpha tocopherol), & vitamin C in Anemia are well known scavengers of free radicals, facilitates the reduction of ROS (Reactive oxygen species) which are free radicals, so it preventing the chain reaction that contributes to oxidative damage G Tocopherol improves cardiovascular function. Vitamin C in Anemia helps is in iron metabolism as it increases the delivery of iron from ferritin & RE system so increases iron use in heme synthesis, so increases red cell formation & decreases the erythrolysis of Rbcs It increases iron absorption. Vitamin C involves in transfer of iron into the blood, as well as mobilising it from iron stores. It converts iron from ferric state with 3 electrons to ssferrous 2+ iron as it acts as electron donar. It is evident from the results that antioxidants taken on a regular basis can bring about significant decrease in the level of Hypertension, Blood Sugar and Lipid Profile, as compared to those who are not taking antioxidants regularly. As Vitamin E & C possesses their greatest potential in the area of stress relief and relaxation. And in the fast pace world in which we live, these findings may prove to be extremely significant and useful in this study, there were statistically significant change in PCV, MCH, MCV, MCHC &RBC count values with and without treatment in control group 3 with insignificant p value .it showed improvement in HB levels with significant p=value. Termination is when a radical reacts with a non-radical, it always produces another radical, which is why the process is called a "chain reaction mechanism". This step is halted in anemia by antioxidants.

CONCLUSION

Most patients in this study had sedentary lifestyle. The low physical activity must be related to hypertension, diabetes, and anaemia. Supplementation of combined doses of Vitamin C & E intake showed some improvements in different basal and blood parameters (PR, BP, PPBS, STC, STG, HDL & levels), in this study it was observed that blood pressure (SBP & DBP) showed improvement after antioxidants pre & post supplementation phase of test group. However, further studies were recommended involving large number of patients from different socio-economic groups with other investigations and further understanding the role of antioxidants in diabetic, hypertensive and anemic patients.

LIMITATIONS

Only antioxidants Vitamin C & E were given in our study& other trace elements as Vitamin D, zinc, selenium, magnesium are not given which may be helpful in supplementation in diabetic, hypertensive & anemic subjects. Further studies are recommended.

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