International Journal of Pharmacological Research
ISSN: 2277-3312
www.ssjournals.com
Journal DOI:10.7439/ijpr

A comparative trial on the efficacy of vitamin c as add on therapy to the oral hypoglycemic agent on serum lipid level in newly diagnosed type 2 diabetes mellitus

Dr. Rekha Nayaka M.R.*

Assistant Professor, Department of Pharmacology, JNMC, Belagavi, Karnataka, India

Corresponding author*
Dr. Rekha Nayaka M.R.
Assistant Professor,
Department of Pharmacology,
JN Medical College, Belagavi.
E-mail: drrekharaghu@gmail.com

Abstract

Background: Diabetic patients are more prone to develop cardiovascular diseases due to rise in blood glucose and serum cholesterol level. There will be elevated free radicals and decreased antioxidants like vitamin C level in these patients. Vitamin C has shown beneficial effect in controlling serum lipids and blood glucose level.
Aim: to study the effect of different doses of Vitamin C on serum lipid level
Methods: A total of 90 patients with newly diagnosed type 2 diabetes referred to Government Hospital, Chennai, India, were included in the study. Patients were divided into 3 groups. They received randomly glibenclamide 5mg, glibenclamide 5mg with vitamin C 1g and glibenclamide 5mg with vitamin C 2g orally for 8-weeks. Investigations like Fasting blood sugar (FBS), Postprandial blood sugar (PPBS), Lipid profile: LDL, HDL, TG, TC were measured before and after vitamin C consumption and the results were analyzed.
Results: Significant increase in HDL level ($p<0.01$)seen in group supplemented with vitamin C 2g when compared to group supplemented with vitamin c 1gm at the end of 8^{th} week. There was significant reduction in TG, LDL and TC level in each group at the end of 8^{th} week but no significant difference in between the groups.
Conclusions: Vitamin C in a dose of 2g/day as add on therapy to oral hypoglycemic agent produces improvement in lipid profile to the desirable levels and thus reducing the risk of diabetic complications.
Keywords: Vitamin C- type 2diabetic mellitus- Serum lipids

1. Introduction

Diabetes mellitus (DM) is a group of syndromes characterized by hyperglycaemia, altered metabolism of lipids, carbohydrates and proteins.[1] The vast majority of patients have type 2 DM .[1] Apart from hyperglycemia, DM is also characterized by oxidative stress, inflammation, and insulin resistance.[2] Several investigators have implicated the role of free radical-mediated pathology in diabetes mellitus.[3,4] Diabetic patients will be having high level of free radicals and low level of antioxidants, including vitamin C. Decreased vitamin C level is associated with increased oxidative stress and hyperglycaemia in diabetic patients.[5] Vitamin C plays important role in prevention of diabetic complications by scavenging free radicals like ROS and RNS, preventing the initiation of chain reactions that lead to protein glycation[6,7], and protecting against lipid peroxidation[6,8]. Vitamin C supplementation has been shown to improve glucose tolerance, lipid profile and reduce cutaneous capillary permeability in Type 2 DM.[9] In current situation diabetes treatment has poor outcome in spite of the best currently available treatments. Hence, development of novel strategies to improve the outcome will be of great benefit. Presently available oral hypoglycemic agents do not show marked improvement in oxidative stress in diabetic patients.[10]

Hence, this study was undertaken to evaluate whether the above mentioned theoretical benefits actually translate into clinically observable benefits in patients of newly diagnosed Type II diabetes mellitus. Glibenclamide, Vitamin C 1g and 2g were used in present study.

2. Materials and Method

This randomized controlled study was carried out in the outpatient Department of Diabetology, Government General Hospital, Chennai, from December 2008 to may 2009. This was a prospective, open label, randomized, Comparative, controlled clinical trial. Patients attending diabetology OPD were invited to participate in the study. The inclusion criteria were: Newly diagnosed Type 2 DM patients with fasting Blood glucose between 140-250mg/dl

(7.8mmol–13.9mmol), of either sex within the age group of 35-65 years. Exclusion criteria were: Patient with Type1DM, Patient with fasting glucose level >250 mg /dl (13.9 mmol), patients with Triglycerides>400mg/dl, Total cholesterol >400mg/dl, LDL >200 mg/dl, patients with DM related complications (Diabetic neuropathy, Diabetic nephropathy, Diabetic retinopathy), Body mass index (BMI) > 30, Patients with hypertension, History of Renal Stones, Patients with evidence of gastrointestinal tract, endocrine, renal, hepatic, cardiovascular abnormalities and any other major systemic illness, Pregnant and lactating women, Patient who cannot comply the protocol, Patient not willing to give written informed consent. The study protocol was approved by the Institute Ethics Committee.

A detailed medical and general physical examination was performed. Patients were enrolled after informed and written consent as per the inclusion and exclusion criteria. Current medical history and diagnosis were noted during the first visit. Patients were randomly assigned into 3 groups with 30 patients in each group. Group I patients received glibenclamide 5 mg twice a day orally for 8 weeks, Group II patients received glibenclamide 5mg twice a day and vitamin C 500mg twice a day orally for 8 weeks, while Group III patients received glibenclamide 5mg twice a day and vitamin C 500mg 4 times /day orally for 8 weeks. After enrollment into the study, follow-up was performed at 4^{th} week and at 8^{th} week. At each follow up visit, fasting, post prandial blood sugar, Lipid profile -LDL, HDL, Total triglyceride (TG), Total cholesterol (TC) were recorded. Investigations such as hemogram (Hb, TLC), serum creatinine, SGOT, SGPT, blood urea, Urine routine: Albumin, microscopic examination, ECG were performed during the first visit and at the end of 8 week of study period. The primary end point was to evaluate efficacy of vitamin C 1g and 2g as an add on therapy to oral hypoglycaemic agent (glibenclamide) on serum lipid level, in newly diagnosed Type 2 diabetes mellitus patients. Patients who did not complete the full 8 weeks of therapy as per the study regulations were not included for statistical analysis. Safety was assessed in terms of subjective systemic adverse effects, Subjective symptoms such as Diarrhea, nausea, vomiting, Giddiness, Fatigue, Headache.

2.2 Statistical analysis

Statistical methods used were Chi-square, paired T-test, and one way ANOVA. $P<0.05$ was considered significant, $P<0.001$ was considered as highly significant, while $P>0.05$ was considered as insignificant.

3. Results

Baselines reading of FBS, PPBS, TG, TC, LDL and HDL in all 3 groups were similar and comparable. Regarding demographic characteristics, parameters such as age distribution($p<0.94$), body mass index($p<0.94$) and sex distribution($p<0.8$)showed no significant difference .Other haematological and biochemical parameters like complete hemogram, blood urea, serum Creatinine, Liver function tests such as SGOT, SGPT, Serum alkaline phosphatase, Total bilirubin, Total protein, albumin were measured at the baseline, at the end of 8^{th} week and found to have no statistical difference among the study groups**.**

At the end of 4^{th} and 8^{th} week serum triglyceride , total cholesterol ,LDL level significantly reduced within the groups but there was no significant difference in improvement between the groups. At the end 8^{th} week ,group II($p=0.0268$) & group III ($p=0.0013$) showed significant increase in HDL level when compared to group I ($p=0.695$).

At the end of 8^{th} week both FBS & PPBS level showed significant reduction within the group and there was significant improvement in PPBS level in group III than group I and group II ($p<0.0279$) but there was no significant difference of FBS level in between the groups.

Table 1: Baseline reading before giving study drug

	Group I (n=28)	Group II (n=28)	Group III (n=27)	p Value
Age(Years)	47.26	48	48.33	p<0.94
BMI	26.8	26.7	26.7	p<0.93
FBS(mg/dl)	184.29	184.31	184.27	p<1.00
PPBS(mg/dl)	220.157	219.210	219.103	P<0.98
TG	193.667	193.767	192.900	p<0.98
TC	209.367	209.133	209.367	p<0.99
LDL	134.377	133.897	131.640	p<0.85
HDL	37.100	37.100	37.000	p<0.99

Table 2: Reading taken at the end of 4^{th} week

	Group I (n=28) mean	Group II (n=28) mean	Group III (n=27) mean	p Value
TG	180.300	177.800	175.033	p<0.7382
TC	194.233	194.333	194.267	p<0.999
LDL	122.430	122.323	120.543	p<0.8751
HDL	37.200	37.767	37.167	p<0.8289
FBS	171.90	171.69	169.06	p < 0.883
PPBS	210.407	210.333	201.590	p<0.242

*p value <0.05 is significant

Table 3: Reading taken at the end of 8th week

	Group I(n=28) mean	Group II(n=28) mean	Group III(n=27) mean	p Value
TG	171.400	170.800	164.600	**p<0.4531**
TC	178.400	173.567	171.000	**p<0.482**
LDL	111.420	109.817	104.973	**p<0.2773**
HDL	37.867	39.967	40.667	**p<0.0188***
FBS	164.31	160.13	155.41	**p < 0.337**
PPBS	198.507	198.033	185.250	**p<0.027***

*p value <0.05 is significant

4. Discussion

Diabetic patients will be having high level of free radicals and low level of antioxidants, including Vitamin C. Low level of vitamin C may be due to lesser intake or increased urinary excretion and defective transport across cell membranes, along with increased oxidation of ascorbic acid to dehydroascorbic acid (DHAA). Defective cell membrane transport of ascorbic acid into vascular epithelial cells (cells that line the inside of blood vessels) when blood sugar is elevated may promote the development of atherosclerosis and angiopathy. The accumulation of DHAA may not only promote the diabetic process but also oxidative damages. Several studies showed oxidative stress is increased mainly due to increased free radicals in diabetes. These free radicals reduce cell membrane responsiveness to insulin and endothelial dysfunction leading to insulin resistance. Free radicals also interfere in the metabolism of lipids leading to high LDL &TG, low HDL levels. This imbalance between free radicals & antioxidant, may contribute to insulin resistance which results in elevated blood glucose level and abnormal lipid metabolism.

Vitamin C supplementation reduces oxidative stress and helps in regulation of lipid metabolism. Vitamin C is structurally similar to glucose and can replace it in many chemical reactions and thus is effective in prevention of non enzymatic glycosylation of proteins, a process that plays an important role in the developments of diabetic complications. Glycosylated proteins & its end products gets deposited in thick basement membrane of vessels leading to microvascular leakage & deactivation of endothelium derived relaxing factor leading to microvascular occlusion. Supplementation of Vitamin C, an antioxidant, reduce the insulin resistance by improving endothelial function and lowering oxidative stress .Vitamin C lowers the sorbitol level in RBCs. This is important because, tissue sorbitol accumulation is associated with the development of diabetic complications including cataract, retinopathy and neuropathy.[11] Clinical trials were conducted to show the effect of vitamin C in reducing fasting blood glucose level & also on lipid profile. In clinical study conducted at Diabetes Research Center, Shahid Sadoughi University Of Medical Seinces, Iran, vitamin C 500 mg & 1000mg were administered for a period of 6 weeks to patients with type 2 DM. Vitamin C 1000mg showed statistically significant reduction in fasting blood glucose & improvement in lipid profile but there was no significant fall in the serum triglyceride level. Forghani *et al*[12] showed significant reduction in serum LDL level in patients supplemented with 1000mg mg /day of vitamin c for 6 weeks. In a study conducted by Erriksons *et al*[13], Finland 2 g of vitamin C for 90 days showed significant reduction in triglyceride in type II Diabetes patients.

Our present study showed that vitamin C 2gm helps in increasing HDL level significantly in group III patients at the end of 8th week and significant reduction in TG, TC, LDL within the groups but no significant reduction in between the groups at the end of 8th week. These results can be confirmed by long term supplementation of vitamin C in diabetic patients. Mild adverse effects such as nausea, vomiting, diarrhea, giddiness, headache, oral mucosal erosion and fatigue occurred among study groups which does not show any statistical significant difference.(P<0.07).

5. Conclusion

Based on the results of our study we can conclude that Vitamin C produces beneficial effect in type II diabetes patients. Vitamin C 2g/day showed improved the lipid profile effectively which helps in reducing the diabetic complications.

References

[1] Afkhami-Ardekani M, Vahidi AR, Borjian L, Borjian L. Effect of vitamin C supplement on glycosilated hemoglobin in patients with type 2 diabetes. *J Shah Sad University* 2003:10:15-8.

[2] Tierney L M, McPhee S J, Papadakis M A. Current medical Diagnosis & Treatment. International edition. New York: Lange Medical Books/McGraw Hill, 1203-1215.
[3] Rother, Kl "Diabetes Treatment-Bridging the Divide". *New England Journal of Medicine* 2007; 356(15): 1499-1501.
[4] Sartoskar RS, Bhandarker SD, and Nirmala, Pharmacology and Pharmacotherapeutics, 20th Edition., Popular Prakasan, Mumbai, India, 2007. Pg no:871 -900.
[5] Von Mehring J, Minkowski O. "Diabetes mellitus nach pankreasexstirpation.". *Arch Exp Pathol Pharmakol* 1890; 26:371-387.
[6] Seidell JC "Obesity, insulin resistance and diabetes-a worldwide epidemic". *British Journal of Nutrition*. 2000; 83 Suppl 1: S5-8.
[7] Ramachandaran A, Snehalatha C, Vijay V.Explosion of type 2 Diabetes in the Indian subcontinent. *International Diabetes Moniter* 2003; 15:1-6.
[8] Ramachandaran A, Snehalatha C, Baskar *et al*. Temporal changes in prevalence of diabetes and impaired glucose tolerance associated with life style transition occurring in rural population of India. *Diabetologica* 2004; 47:860-863.
[9] Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030". *Diabetes Care* 2004; 27(5): 1047–53.
[10] "Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications" WHO,
[11] Journal from June 14, 2006, Diabetes Research Center, Shahid Sadoughi University of Medical Sciences & Health Services, Yazd, Iran.
[12] Forghani B, Goharian V, Kassayian N, Amini M. The effect of vitamin C supplements on serum lipoprotein levels in NIDDM patients. *J M C Isfahan Univ* 2001; 2: 95-100.
[13] Errikson J, Kahvakka A. Magnesium and ascorbic acid supplementation in diabetes mellitus. *Ann Nutr Metab* 1995; 39: 217-23.