Effect of Ascorbic Acid on Dyslipidemia (a study among Philippine Heart Center Employees)

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Background **---** Hypercholesterolemia is one of the risk factors for coronary artery disease. Chronic dietary inadequacy of vitamin C affects not only plasma cholesterol and triglyceride concentrations but also the integrity of the vascular wall. The tendency of low density lipoprotein [LDL] to oxidation is surmised to be a critical factor responsible for atherogenesis. There is substantial evidence for a role of dietary antioxidants in the prevention of atherogenesis, which may be mediated through inhibition of the oxidative modification of LDL and the most effective way is to ensure maximal steady-state levels of ascorbate in the tissues. Triglycerides were also a strong independent risk factor for predicting coronary heart disease. Therefore, based on these facts, the purpose of this study is to investigate the effectiveness of ascorbic acid supplementation on levels of total cholesterol, LDL-C, HDL-C and triglycerides.

Methods **---** An open non-comparative experimental study was done to 59 Philippine Heart Center employees 20 years old and above who have elevated serum cholesterol level and with 0 to 1 risk factor based on National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) guidelines. They were given 2,000 mg of ascorbic acid daily for 3 months. At the end of 3rd month, lipid profile was repeated and compared with levels obtained from baseline. There were no specific diet modifications during the entire study period except that which have been given by the infirmarian. Patients who are taking any kind of multivitamins were advised to discontinue it temporarily to avoid interference with the result.

Results **---** The mean baseline total cholesterol, LDL, triglycerides, and HDL level were 226.32 mg/dL, 139.95 mg/dL, 110.81 mg/dL, and 59.64 mg/dL respectively. For total cholesterol, the mean effective change after Vitamin C supplementation was 38.49 mg/dL [SD ±11.73; p= 0.002], while for LDL cholesterol, the mean effective change was 23.39 mg/dL [SD ± 7.49; p= 0.003]. For triglycerides, the mean effective change was 25.85mg/dL [SD ± 8.72]; p= 0.004]; whereas, for HDL cholesterol, the mean change shows a decrease of 11.92 mg/dL [SD ± 3.71; p= 0.002].

Conclusions **---** This study indicates that supplementation with 2 grams of vitamin C daily for 3 months results to a significant decrease in serum total cholesterol, LDL-C and triglyceride concentrations. However, there was also a significant reduction in the HDL-C level. Although there was a negative change in HDL-C levels, changes on total cholesterol, LDL-C and triglycerides can have beneficial effects on the incidence of coronary heart disease when supplementing vitamin C within the non-toxic range.

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Hypercholesterolemia is one of the risk factors for coronary artery disease. Lipid oxidation and propagation of free radicals may contribute to the development of atherosclerosis. To prevent the oxygen radicals from producing damage, antioxidants act by neutralizing this free radicals by allowing the pairing of electrons.[1]

Several nutritional compounds has been shown to reduce total serum cholesterol concentration; one of these compounds is ascorbic acid.

Ascorbic acid or vitamin C is the main water-soluble antioxidant in human plasma.[2] It is involved in the regulation of choles-

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terol metabolism in several ways. Low plasma Vitamin C level affects the cholesterol and triglyceride concentration; and if this becomes persistent, the integrity of the vascular wall will be affected.[2]

The susceptibility of low density lipoprotein [LDL] to oxidation is thought to be a crucial factor responsible for atherogenesis. There is evidence that dietary antioxidants could prevent atherogenesis by inhibiting the oxidative modification of LDL; and the most effective way to achieve this is to maintain the maximal steady state level of ascorbic acid in the tissue.[2]

The role of triglyceride in the development of coronary artery disease was proven by the Copenhagen study. The study shows that triglycerides are actually a strong predictor of coronary heart disease.[3] This finding was supported by a meta-analysis of 17 population-based prospective studies.[4]

Several studies strongly suggest that chronic inadequacy of vitamin C level on plasma leads to hypercholesterolemia and accumulation of cholesterol on certain tissues.[5] Low vitamin C level indirectly decreases cholesterol absorption due to low levels of bile acids, monoglycerides, and fatty acids.[5]

In experimental studies involving animals, ascorbic acid has been found to be important in cholesterol homeostasis. Studies have reported that ascorbic acid administration decreases blood cholesterol level in guinea pig, an animal, like humans, lacks the enzyme necessary for hepatic synthesis of ascorbic acid.[6-8] It has been shown that ascorbic acid is important for the conversion of cholesterol to bile acids.[9-11]

Several trials have shown that administration of vitamin C to individuals with total serum cholesterol >200 mg/dl could lower its level, especially in those individuals with less than full tissue saturation of ascorbic acid.[12]

This study aims to determine the effect of 2 gram ascorbic acid supplementation on the lipid levels.

Methodology

This is an open-label non-comparative experimental study involving Philippine Heart Center employees 20 years old and above, who have elevated serum cholesterol level and with 0-1 risk factor based on NCEP-ATP III guidelines. Excluded were those with history of cerebrovascular disease; those with history of coronary artery disease, such as those with history of acute coronary syndrome, chronic stable angina, or with established coronary artery disease based on coronary angiogram findings; those who have contraindications to ascorbic acid; those who are already using statins; those with total cholesterol level of $\geq$ 240 mg/dl; those with triglyceride level of $\geq$ 200 mg/dl; and those with LDL cholesterol level of $\geq$ 190 mg/dl. This study was approved by the institutional review board and informed consent was obtained on all subjects.

All enrolled subjects had a baseline lipid profile determination They were given 2,000 mg ascorbic acid daily for 3 months. At the end of the hird month, the lipid profile was repeated and compared with levels obtained from baseline. There were no specific diet modifications during the entire study period, except those which was given by the infirmarian. Patients who are taking any kind of multivitamins were advised to discontinue it temporarily to avoid interference with the result.

Statistical Analysis. Qualitative data was expressed as frequency and percentage, while quantitative data was expressed as mean and standard deviation. Mean difference was obtained for all the lipid profile levels. A p-value of 0.05 was considered significant. Data was analyzed using STATA 11.

Sample size computed is 60 patients. The assumption was based on the meta-analysis done by McRae with assumed effect size of 1.1 ± 2.1 at $\alpha = 0.05$ and $\beta = 0.20$.

Results

Table 1. Baseline characteristics of PHC employees with dyslipidemia included in the study (PHC, 2010)

Characteristics	n(%)/mean ± SD n=51
Age (years)	41.63 ± 8.93
Male	18 (30)
Female	41 (70)
Hypertension	13 (22)
Smoker	5 (8)
Hypothyroidism	1 (2)
BMI*	
<18.5	0
18.5 - 24.9	23 (39)
25 - 25.9	24 (41)
30 - 39.9	12 (20)
≥40	0
SBP	116.78 ± 10.99
DBP	76.78 ± 8.80

* based on Asia - Pacific BMI

Fifty-nine (59) subjects were enrolled in the study. The mean age was 41.63 years and majority was females (70%). Thirteen (13) subjects were hypertensives, five (5) were smoker, and one (1) had hypothyroidism. Most of the subjects (41%). belong to the overweight group.

During the study period of twelve weeks, 13 out of 59 enrolled subjects prematurely stopped taking Vitamin C 2 grams daily. Four (4) subjects experienced dizziness, three (3) subjects claimed that their appetites increased, and nine (9) subjects developed epigastric pain. All of these nine subjects discontinued the study drug. Four (4) subjects stopped the medication without any reason.

The mean baseline total cholesterol, LDL, triglycerides, and HDL level were 226.32 mg/dL, 139.95 mg/dL, 110.81 mg/dL, and 59.64 mg/dL respectively.

The mean change between baseline and post-treatment total cholesterol, LDL, triglycerides and HDL level are presented in Table 2. For total cholesterol, the mean effective change of vitamin C supplementation was 38.49 mg/dL [SD ±11.73; P= 0.002]. For LDL cholesterol, the mean effective change was 23.39 mg/dL [SD ±7.49; P= 0.003]. For triglycerides, the mean effective change was 25.85 mg/dL [SD ±8.72]; p= 0.004]. For HDL cholesterol, the mean change shows a decreased of 11.92 mg/dL [SD ±3.71; p= 0.002].

Discussion

In this study, 2 grams of vitamin C supplementation provided a significant reduction in total cholesterol (38.49 mg/dL), LDL (23.39 mg/dL), and triglycerides (28.85 mg/dL), but failed to show an increase in HDL cholesterol level; instead, it reduces HDL levels by 11.92 mg/dL. This last result is in contrast with several trials that vitamin C intake positively correlates with HDL cholesterol concentration. [13-17]

One possible reason for this is because plasma vitamin C levels were not high enough to produce positive effect on HDL

Table 2. Lipid levels before and after intake of Ascorbic Acid Lipid levels of PHC employees with dyslipidemia before and after administration of 2g Ascorbic Acid for 3 months (PHC, 2010)

Lipid	Pre-Treatment mean ± SD	Post-Treatment mean ± SD	Difference mean ± SD	p-value
Total Cholesterol, mg/dL	226.32 ± 4.46	187.83 ± 12.47	38.49 ± 11.73	0.002
HDL, mg/dL	59.64 ± 4.40	47.73 ± 4.74	11.92 ± 3.71	0.002
LDL, mg/dL	139.95 ± 3.19	116.56 ± 8.00	23.39 ± 7.49	0.003
Triglycerides, mg/dL	110.81 ± 6.88	84.97 ± 8.20	25.85 ± 8.72	0.004

cholesterol. A pooled analysis of nine (9) cohort studies found that those who took at least 700 mg of vitamin C had a 25% reduction in the incidence of coronary heart disease.[18] Majority of the studied populations are men, and women are less represented. Recent evidence from primary prevention trials in predominantly male population shows that CHD incidence can be reduced to 31% to 37% by 25% LDL-C reductions from levels of 4 to 5 mmol.[19-20] In this study, majority of the enrolled population were female (70%) and this result suggest that both gender would benefit by achieving low LDL-C levels.

The mean change in triglyceride levels as a result of Vitamin C supplementation of 2 g daily was greater compared with LDL-C (25.85 mg/dL vs. 23.39 mg/dL). This observation is of particular interest because the literature on vitamin C mechanism and actions focused primarily on changes in HDL and LDL-C. In a review paper done by Hemila, he did comprehensively explained the vitamin C's ability to decrease triglyceride levels. In the data examined by Hemila,the weighted decrease in triglycerides was approximately 8% when compared to control group.[21] Consistent with a recent review, triglyceride was associated with greater risk reduction in women (4.7) than in men (2.1).[22]

It has been shown that LDL to HDL ratio is a good predictor of coronary heart disease.[23] In this analysis, there was an increase in the LDL/HDL ratio [-0.10]. When compared with the baseline level, this equates to a 4.27% increase from baseline. This increase could be explained by a decrease in HDL-C level post-treatment. The triglyceride to HDL ratio is also a good predictor of coronary artery disease, and in this study, the average decrease in the triglyceride HDL ratio was 0.07. When compared with the baseline, this equates to 3.78% reduction from baseline.

Although there was an opposite result in the triglyceride/HDL ratio and LDL/HDL ratio,[24] this could still account for a similar change in coronary heart risk because it has been shown that the LDL/HDL ratio may underestimate coronary heart disease risk when compared with the estimation achieved with the triglyceride to HDL ratio.[25]

This study has several limitations. First, the study design used was an open non-comparative experimental study, a study design inferior to a randomized controlled trial. Second, plasma vitamin C concentrations were not obtained from subjects; hence, the total serum vitamin C concentrations were not identified. Third, recruited patients may have different dietary habits that may affect both the starting baseline total cholesterol level as well as the absorption of the vitamin C supplement that is dependent upon the initial plasma concentration of ascorbic acid.

Conclusion

This study indicates that supplementation with 2 grams of vitamin C for 12 weeks can result to a significant decrease in serum total cholesterol, LDL-C and triglyceride concentrations. However, there was also a significant reduction in the HDL-C level. Although there was a negative change on HDL-C, changes on total cholesterol, LDL-C and triglycerides can have beneficial effects on the incidence of coronary heart disease, especially in the light of the low cost and when supplementing vitamin C within the non-toxic range.

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