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Full Length Research Article

Effects of Folic Acid Intake on Serum Lipid Profiles of Apparently Healthy Young Adult Male Nigerians

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ABSTRACT
The effects of folic acid intake on serum lipid profile of apparently healthy young adult males were investigated. Ten apparently healthy young adult males (19-22years) were requested to observe 10-12h overnight fast prior to the days of appointment. Blood samples were collected 1h after the intake of appropriate volume of physiological saline (control), 5mg and 10mg of folic acid respectively at 4days interval. Compared with the control, 5mg and 10mg folic acid resulted in similar pattern of significant reduction in serum cholesterol and LDL-C ($p<0.05$) while there was large scale increase in HDL-C ($P<0.05$). Furthermore, the intake of 5mg folic acid produced significant increase in triacylglycerol while the 10mg folic acid intake resulted in significant decrease in serum triacylglycerol concentration ($P<0.05$). These results indicate that folic acid supplementation may provide additional benefit to humans since it increases the blood level of good cholesterol (HDL-C) and reduces the blood level of 'bad' cholesterol. These effects are additional to the well known haematological benefits of folic acid supplementation.

Keywords: *folic acid, cholesterol, triacylglycerol, serum, Nigeria*

INTRODUCTION

Folic acid (folinic of foliacin) first isolated from Spinach leaves is a compound composed of a heterocycle, p-aminobenzoic acid and glutamic acid. Various forms of folic acid are present in a wide variety of plants and animal tissues; the richest sources are yeast, liver, kidney and green vegetables (Green and Miller, 1999). It can undergo reduction catalyzed by the enzyme dihydrofolate reductase to give dihydrofolic acid-Tetrahydrofolate. It is required for the formation of creatinine and choline, the synthesis of purine and the methylation of RNA. It is also needed for the proper metabolism of the essential amino acid, methionine found primarily in animal protein (Moustapha and Robinson, 1999). Folic acid like other vitamins is an essential part of human diet to promote good health (Katzung, 2000).

Folic acid deficiency which is often caused by inadequate dietary intake of folates, alcoholism, liver diseases and consumption of drugs like phenytoin, oral contraceptives and isoniazid (Dastur and Dave, 1987; Katzung, 2000) could result in Alzheimer's disease, increased rate of heart diseases, strokes, depression and dementia among others (Morrison, 1996; Albert and Fava , 1997; Snowdon *et al*, 2000).

Elevated plasma homocysteine levels have been linked with higher incidence of cardiovascular diseases (Moustapha and Robinson, 1999; Assanelli *et al*., 2004) and in patients with hyperhomocysteinemia and myocardial infarction, folic acid supplementation has been found to significantly decrease the

homocysteine level and improved arterial endothelial function (Lawrence, 2000; Nelson and Cox, 2000; Assanelli *et al*., 2004). Studies have shown that a folate-rich diet is as effective as folic acid from supplements in decreasing plasma homocysteine concentrations in hyperhomocysteinemia and coronary artery diseased patients (Pinto *et al.,* 2005). Studies have also shown that folic acid improves endothelial function in coronary artery disease via mechanism largely independent of homocysteine lowering (Doshi *et al*., 2002). However, most of these studies did not take care of the effect of oral administration of folic acid at the doses investigated in this study and on the lipid profile of apparently healthy humans, which was the focus of this study. Furthermore, the study was designed to investigate whether the beneficial effect of foliate supplementation on coronary artery disease could be due to a combination of changes in serum lipid profiles as well as homocysteine. In addition, most of the available studies (to the best of our knowledge) did not provide any information on Nigerians. Therefore, this study was also carried out in order to assess the effect of folic acid supplementation on the lipid profiles of apparently healthy young adult Nigerian males.

MATERIALS AND METHODS

Study Design

The subjects that participated in this study were properly briefed on the rationale and the requirements of the study. Each subject gave informed consent to participate in the study which complies with the ethical rules on human and animal experimentation and approved by the Ethical Committee, College of Medicine, University of Ilorin, Ilorin, Nigeria. Each subject was requested to observe 10-12h overnight fast prior to the days of appointment. Blood samples were collected on the 1st day, 4th day and 8th day of appointment corresponding to the control in which appropriate volume of physiological saline was orally administered, those in which 5mg of folic was orally administered and the 8th day corresponding to oral administration of 10mg folic acid. In each case, venous blood samples were collected 1hr after the administration of the chemical compounds.

Ten apparently healthy adult males between the ages of 19-22years with an average age and weight of 20.5±0.85 and 61.4±6.52 respectively, all being students of University of Ilorin, Ilorin, Nigeria were recruited for the study with selection criteria carefully applied. The anthropometric measurement was determined. Folic acid was obtained from Meyers Pharmaceuticals, Lagos, Nigeria. The assay kits for Total Cholesterol, High density lipoprotein (HDL-C), Low density lipoprotein cholesterol (LDL-C) and Triglyceride were obtained from Quinica Clinica Applicada, S.A, Spain. All other reagents used were of analytical grade.

Blood Collection

The subjects were made to sit comfortably; tourniquet which serves to constrict the veins so that blood flow was reduced in the part below the constriction was tied around the upper arm. The skin was cleansed with methylated spirit and cotton wool after which the syringe and needle was carefully driven into the vein. The plunger was pulled to withdraw about 5ml of blood. This was collected into centrifuge tubes after which it was centrifuged at 3000rpm for 5mins (Ogbu and Okechukwu, 2001). Serum was removed from the clotted blood using Pasteur pipette. The serum was then analysed for the total cholesterol, HDL-C, LDL-C and triglyceride levels.

Determination of lipid profile

The total serum cholesterol was determined by the Pap-method as previously described (Fredrickson *et al*., 1967). LDL-Cholesterol was determined based on the Polyvinylsulphate method (Demacker *et al*., 1984). Serum HDL-Cholesterol estimation was based on Dextran sulphate-Mg^{2+} method (Albers *et al*., 1978) while the serum triglyceride content was determined using the procedure of glycerol-phosphate oxidase as was reported (Fossati and Prencipe , 1982).

Statistical Analysis

Statistical analysis of data was by the Student t-test and differences were considered significant at $P<0.05$ (Woodson, 1987).

RESULTS

The effects of acute intake of folic acid on the lipid profile of apparently healthy young adult males are shown in Table 1. Compared with the control, intake of 5mg and 10mg folic acid resulted in significant reduction in the serum total cholesterol and LDL-C concentrations ($P<0.05$), with that of 10mg folic acid producing half the control values. However, the intake of 10mg folic acid produced values of total cholesterol and LDL-C that were significantly reduced when compared with the 5mg folic acid intake ($P<0.05$). The two doses (5mg and 10mg) produced contrasting pattern on serum

triglyceride content with that of 5mg folic acid producing significant increase of about two and a half times the control (P<0.05) whereas the 10mg intake produced significant decrease of about half the control value (P<0.05). On the other hand, intake of folic acid (5mg and 10mg) resulted in a significant increase in serum HDL-C content when compared with the control (P<0.05).

Table I:
Effect of intake of 5mg and 10mg folic acid on the lipid profile of apparently healthy young adult males.

Parameters	Control	5mg	10mg
Total Cholesterol (mmol/L)	4.40 ±0.36	3.54 ±0.23**[a]	3.12 ±0.42**[b]
LDL-C (mmol/L)	2.16 ±0.26	1.37 ±0.15**[a]	1.10 ±0.14**[b]
Triglycerides (mmol/L)	0.79 ±0.12	1.77 ±0.50**[a]	0.41 ±0.12**[b]
HDL-C (mmol/L)	0.96 ±0.20	1.74 ±0.19**[a]	1.71 ±0.21**[a]

*Values are expressed as mean of 10 determinations ±SD, *P>0.05, **P<0.05).*
Mean in each row for each determination with different letters are different (P<0.05).

DISCUSSION

The effects of acute intake of folic acid on principal serum lipids were evaluated in this study because of the possible role of folic acid on tissue metabolism. Such tissue metabolism is likely to involve biochemical reactions or pathways that often determine serum lipid profile in health or disease (Robert *et al*., 2002). Therefore, the hypocholesterolaemia observed in this study (Table 1) may be important in this respect.

The hypocholesterolaemia observed in this study (Table 1) following the acute consumption of folic acids (5mg and 10mg) may be attributed to reduction in the concentration of acetyl CoA resulting from decreased ß-oxidation of fatty acids, since acetyl CoA is a key substrate in the biosynthesis of cholesterol (Rang *et al*., 1995). However, acetyl CoA level was not measured; nevertheless, the hypocholesterolaemia is beneficial as it may help reduce the incidence of arteriosclerosis and hypertension since the two diseased states are associated with high LDL-Cholesterol (Enas, 1999).

The significant reduction in the serum content of LDL-Cholesterol is understandable since a reduction in Total Cholesterol should normally result in reduction in LDL-Cholesterol. This may be adduced to a possible alteration in the catabolism of VLDL since LDL represents the final stage in the catabolism of LDL (Mayes, 1996). The reduction in LDL following the intake of folic acid is of beneficial effect since numerous epidemiological studies have shown that elevated levels of low-density lipoprotein cholesterol are associated with an increased risk of coronary heart disease (Nelson and Cox , 2000; Woo *et al*., 2002).

The increase in high density lipoprotein-cholesterol (HDL-C), also known as 'good cholesterol' following the intake of folic acid (5mg and 10mg) may also be clinically beneficial. This view is in consonant with the reported finding where an increase in the concentration of HDL-C correlates inversely with coronary heart disease (Philip, 1995). The biochemical importance of HDL-C is in the fact that it removes cellular cholesterol, transferring it to the liver for excretion (Mayes, 1996).

The significant increase in triglycerides, (the main storage fatty acids) following the intake of 5mg folic acid may be adduced to accelerated lipolysis. However, the intake of 10mg folic acid produced a contrasting effect (Table I). This might be due to the inhibitory effect on lipolysis.

Although, folic acid supplementation has been found to lower plasma homocysteine level and ultimately reduce the incidence of cardiovascular diseases. The present study shows that folic acid can also reduce one of the risk factors (LDL-C) of cardiovascular diseases through its action on serum lipids. Nevertheless, the clinical application of these findings must await further studies.

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