Folic Acid Treatment of Hyperhomocysteinemia in Dialysis Patients

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Abstract

Objectives: We examined the effect of Folic Acid (FA) administration on the homocysteine level of chronic hemodialysis patients.

Methods: The study group included 16 patients (11 male and 5 female) with CRF; their ages ranged from 20 to 57 years, who were undergoing dialysis at the dialysis unit of Zaid Bin AI-Hussein Hospital in Jordan (2004/2005).

Results: (Hcy) level, of patients' group after supplementation with (FA) led to a significant decrease in homocysteine level (39.7%), ($p<0.001$),while no significant difference in homocysteine level was shown in control patients .

Conclusion: Supplementation of the diet with (FA), at levels above the current recommended dietary allowances, reduces elevated homocysteine levels in (CRF) patients.

Keywords: Homocysteine (Hcy), Folic Acid (FA), Chronic Renal Failure (CRF).

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Introduction

Higher circulating levels of homocysteine are associated with increased risks of vascular diseases, including cerebrovascular disease and peripheral arterial disease as well as other complications of atherosclerosis which are the usual causes of death in patients with chronic renal failure. Hyperhomocysteinemia is a well-recognized risk factor for accelerated atherosclerosis in hemodialysis patients. We measured fasting total plasma Homocysteine (Hcy) in sixteen chronic hemodialysis patients, Folic acid (5 mg/d), were administered for six weeks in Eleven patients receiving dialysis, and the other patients were left as control group.

The eleven patients on treatment with (5 mg) FA daily displayed simultaneous, statistically significant reduction in the concentration of homocysteine (23. 0± 5.2 umol/L), than the controls (34.5 ±6.2 umol/L).

The plasma (FA) concentrations in these groups were (59.0±15.7) and (19.0±4.0) nmol/1, respectively; further studies on the optimal treatment of hyperhomocysteinemia in chronic dialysis patients are needed.

Hyperhomocysteinemia, increased oxidative stress, endothelial activation/dysfunction, and coagulation activation are considered integral components of the inflammatory response. [7]

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Patients with Chronic Renal Failure (CRF) undergoing dialysis have a higher mortality rate due to ischemic heart disease and other complications of atherosclerosis than does the general population. [3] Studies in (CRF) patients show disequilibrium between free radical generating systems and the production of antioxidants. [5] Because oxidative stress is associated with renal failure, it accelerates atherosclerosis and exaggerates the anemia of kidney disease. Hyperhomocysteinemia in these patients should be viewed not only as the probably cause of vascular damage but also as an aggravating factor with respect to the status and prognosis of renal failure. [2]

Other factors are more specific to uremia such as the accumulation of homocysteine and asymmetric dimethylarginine (endogenous inhibitor) which may impair endothelial function. Modulation of endothelial function in (CRF) may offer a novel strategy to reduce cardiovascular disease". Therefore, we believe that folic acid reducing the concentration of homocysteine have inhibited the inflammatory process in vessels, thereby improved functional parameters in renal failure.

Materials and Methods

The study group included 16 patients (11 males and 5 females) with CRF; their ages ranged from 20 to 57 years, who were undergoing dialysis at the dialysis unit of Zaid Bin AI-Hussein Hospital in Jordan.

Their plasma (Hey) was measured postdialysis after an overnight fast, and 11 patients were then created with Folic Acid (FA), 5 mg daily for 6 weeks, plasma (FA) concentrations were measured before treatment and after 6 weeks of follow-up. For (Hcy) measurements, venous blood samples were taken in EDTA-containing tubes that were immediately stored in ice. Plasma was separated within 30 min and stored at - 20°C until analyzed. Hey was measured by Abbott IMx homocysteine assay (normal Hey values in the fasting state at our laboratory, 5-12 umol/L.Plasma Folate was determined by using the Abbott IMx microparticle enzyme immunoassay (data obtained were analyzed by using Mann-Withney U Test on SPSS program). The normal range of plasma (FA) was (3.4 - 38.3 nmol/1). Mean within run and between-run precision were determined to be 1.36% CV, detection limit was found to be linear up to 200). Mol/L for homocysteine.

Results

Fasting total plasma homocysteine (Hey) was markedly increased about 3.2 fold above normal in patients requiring chronic dialysis, while as shown in table (1) (Hcy) level, of patients' group after supplementation with (FA) led to a significant decrease in homocysteine level (39.7%), ($p<0.001$), while no significant difference in homocysteine level was shown in control patients. On the other hand, there was no significant difference in total cholesterol, HDL and LDL, triglyceride, urea, creatinine, and uric acid concentrations before or after supplementation with (FA).

Table 1: Effects of 6 Weeks' Supplementation of Folic Acid on (Hcy) in Dialysis Patients.

Variable	*Before Treatment in (16) Dialysis Patients*	*With out Treatment in (5) Dialysis Patients: Controls*	*After Treatment in (11) Dialysis Patients*	*P*
Homocysteine (umol/L)	*36.5 ±4.1*	*37.5 ±6.2*	*23,0± 5.2*	*< ,001*
Total cholesterol (mg/dL)	*165.2 ±39.2*	*164.2 ±35.1*	*161.5 ±32.6*	*NS*
Triglycerides (mg/dL)	*142.1 ±42.8*	*145.1 ±46.3*	*138.8± 52.4*	*< ,001*
LDL cholesterol (mg/dL)	*138.5 ±35.1*	*136.5 ±31.1*	*142.5± 32.8*	*NS*
HDL cholesterol (mg/dL)	*38.2 ±7.1*	*39.2 ±6.1*	*39.2 ± 7.2*	*NS*
Creatinine (mg/dL)	*7.7 ± 3.5*	*7.6 ± 2.4*	*7.4 ±2.8*	*NS*
Urea (mg/dL)	*72.3 ±21.2*	*70.3 ±21.5*	*70.0 ±22.3*	*NS*
Uric acid (mg/dL)	*7.5 ± 3.8*	*7.2 ± 32*	*7.3 ± 3.9*	*< ,001*
Folic acid(nmol/1)	*(19.0±4.0)*	*(17.50±5.2)*	*(59.0±15.7)*	*< ,001*

Discussion

Elevated blood levels of homocysteine have been associated with an increase risk in the development of vascular disease, neural tube defects and coronary heart disease. Folate is an important cofactor for homocysteine metabolism. Many studies have demonstrated that intakes of foliate are associated with hormone levels that are associated with heart disease risk. [6]

This study examined the relationship between intakes of foliate, and the elevated blood levels of homocysteine in (CRF) patients' plasma. Folic Acid (FA) concentrations were normal in the dialysis group, but these levels of folic acid are not enough to reduce hyperhomocysteinemia in CRF2. Our present results evaluate the influence of (FA) therapy on the concentration of some biochemical risk factors of atherosclerosis in view of the anticipated reduction in morbidity and mortality due to vascular diseases in (CRF) patients. In fact, this suggestion is concordant with the recent opinion of the American heart association on homocysteine. [9]

A positive correlation between the decreases in concentrations of homocysteine after treatment with (FA) was found in most countries, patients undergoing dialysis routinely receive supplementation with water-soluble vitamins. Often this supplementation doesn't protect against hyperhomocysteinemia, possibly because the usual daily doses of folic acid (1 mg), are too low. On the other hand, it remains to be established whether long-term supplementation with high doses of (FA) and B vitamins, often for the lifetime of the patient, is safe. The doses we used were similar to those reported by Bostom et al. [4] A was the approximate 35% reduction in homocysteine levels in our patients who had not previously received high doses (FA) supplementation. To help increase folic acid intake, the US Food and Drug Administration ruled that the fortification of grain and grain products with folic acid be required.

There has been controversy as to whether vitamin [B.sub.12] should be added to these foods as well. The rationale behind this is that the sole addition of folic acid may mask a vitamin [B.sub.12] deficiency, which may lead to irreversible nerve damage. A recent study compares the homocysteine-lowering capability of folic acid with that of supplements containing different amounts of vitamin [B.sub.12] and folic acid. [1]

Conclusion

Hyperhomocysteinaemia is common in renal failure patients. The results suggest that (FA) supplementation has an effect on risk factors of atherosclerosis in patients with renal failure and that interactions may exist between homocysteine and (FA). Supplementation of the diet with (FA), at levels above the current recommended dietary allowances, reduces elevated homocysteine levels. Therefore, the current level of folic acid fortification of foods is insufficient to reduce plasma homocysteine levels significantly in (CRF) patients. Such a reduction could be achieved with a supplemental folic acid intake five to six times the current fortification level.

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