

PROSPECTIVE RANDOMISED STUDY OF HOMOCYSTEINE LOWERING VITAMINS IN SEVERE CARDIOVASCULAR DISEASES

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ABSTRACT

Elevated plasma total homocysteine has been identified as an independent risk factor for vascular disease. Our study aim is to analyse the risk of total homocysteine levels for cardiovascular disease and to estimate the potential reduction of cardiovascular disorders mortality by increasing homocysteine lowering vitamins intake. in order to assess efficacy of plasma total homocysteine levels (fasting), 9 CVD patients were randomly assigned and provided with folic acid (5mg), methylcobalamine (500 mcg), pyridoxine (10 mg) All the patients were treated for 3 weeks and fasting totalHCY were measured before and after treatment. 3 healthy volunteers served as normal control group of study. in our randomised study, after administration of

folic acid alone in group 1 results in a mean reduction of level o totalHCY f 3.8mol /L and folic acid and methylcobalamine in group 11 produced a mean reduction of 3.8mol/L and folic acid and methylcobalamine in group 11 produced a mean reduction of They level 6.7mol/L. while in group 111, by co-administration of folic acid, methylcobalamine and pyridoxine results in in a significant mean reduction of 7.1mol/L implies the significant of folic acid, methylcobalamine, pyridoxine as homocysteine lowering vitamins. Lowering serum concentration of homocysteine has been proven to reduce the risk of adverse cardiovascular events among peoples. our study supports the co-administration of folic acid, methylcobalamine and pyridoxine as homocysteine lowering vitamins in cardiovascular disease. This method could be a therapeutic strategy to combat the risk of cardiovascular disease.

KEYWORDS: Total homocysteine, methylcobalamine, pyridoxine.

MATERIALS AND METHOD

SCOPE OF STUDY

Folic acid other B vitamins help in break down homocysteine in the body. homocysteine levels in the blood are strongly influenced by diet and genetic factors. the American heart association had advised healthy , balanced diet that is rich in fruits and vegetables , whole grains and fat – free or low – fat diary products. So far, no controlled treatment study has shown that folic acid supplementation reduces the risk of CVD. researches are trying to find out how much folic acid , vitamin B6 , vitamin B12 are needed to lower homocysteine levels. screening for homocysteine levels in the blood may be useful in patients with personal or family history of CVD but who do not have the well established risk factors. Although evidence for the benefit of lowering homocysteine levels is lacking , patients at high risk should be strongly advised to be sure get enough acid , vit-B6 and Vit-B12 in their diet . they should eat fruits and green leafy vegetables daily.

OBJECTIVES

- The proposed study was decided to achieve the following objectives
- To determine the risk of total homocysteine levels in cardiovascular diseases
- To estimate the potential reduction of cardiovascular disorder mortality by increasing homocysteine lowering vitamin intakes.
- To analyse the diagnostic criteria for hyperhomocytinemia

METHODOLOGY

SITE OF STUDY

The study was conducted at private hospital. it is a 150- bedded hospital . This study was decided to be conducted in the department of cardiology.

INCLUSION CRITERIA

- Patients with cardiovascular disease
- Normal healthy persons without cardiovascular disease
- Patients before treatment with homocysteine lowering vitamins

EXCLUSION CRITERIA

- Known history of DM
- Patients with serious systemic disorder

- Smokers
- Alcoholics
- Specific interaction for or CI to a study drug or drug procedure

LITERATURE SURVEY

An extensive literature survey was carried out regarding the study of homocysteine lowering vitamins in severe cardiovascular diseases. The various sources of literature include British medical journal, journal of American medical association Asian journal of clinical cardiology etc.

STUDY DESIGN

The study was carried out for a period of six months from march 2012 to August 2012 . This was a randomized placebo controlled single blind study with three active treatments: Group : Folic acid (5mg) ,Group 11: Folic acid (5mg) + methylcobalamin (500mcg) , Group 111 : Folic acid (5mg)+ methylcobalamine (500mcg) + pyridoxine (10 mg)

PHASE 1

Preliminary literature survey

- Pilot scale study : a pilot scale study was carried out a period 10 days in the department of cardiology and the scope of study in that department.

PHASE 2

- Obtaining consent from hospital authority : the protocol of the study which includes the objective , methodology was submitted to hospital.
- Literature survey: Literature, which supports the study was collected and they were properly received for the study of homosystiene lowering vitamin in severe cardiovascular disease.

PHASE 3

- Data collection: The patients details was collected before and after the treatment and recorded
- Data Analysis: The collected data from the patients were thoroughly analysed and concluded the results.
- Reports and Submissions: The data which were collected, categorized and analyzed made as a report.

RESULTS

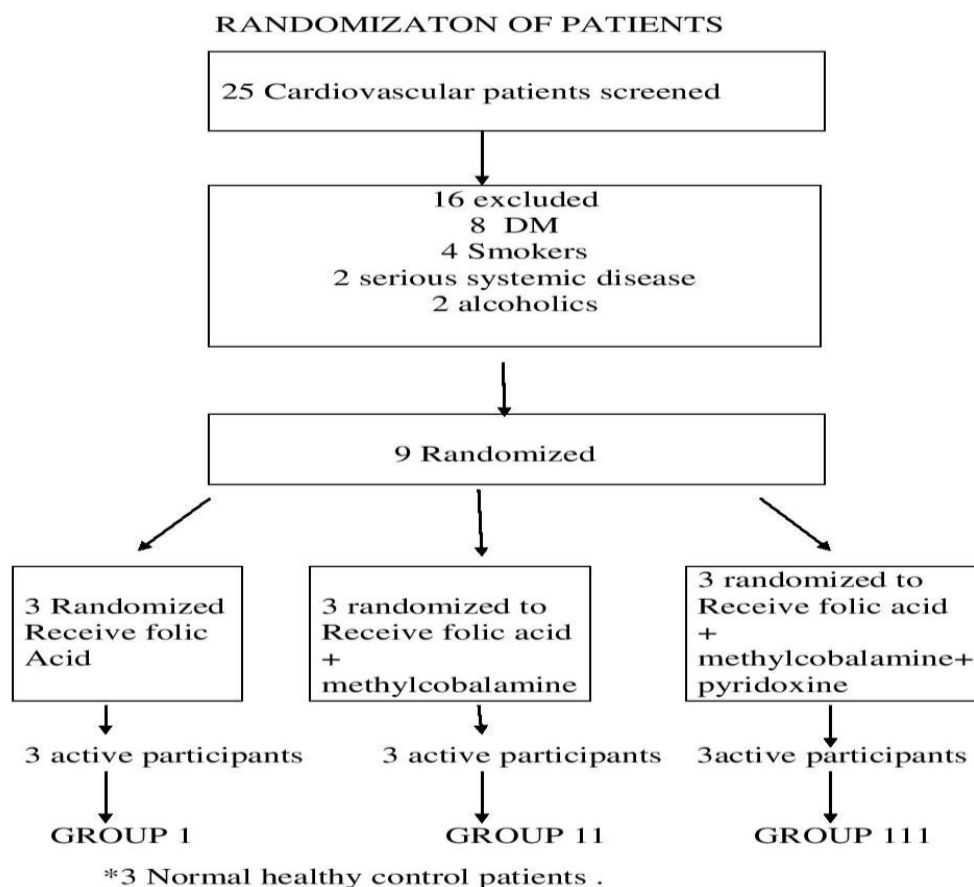
Out of 25 CVD patients selected 16 patients were excluded from the study due to co-morbid diseases like DM, serious systemic disorders, alcoholics, smokers etc. from the 16 excluded 32% were DM patients (n=8) , 16% were smokers (n = 4) 8% serious systemic disease (n=2) and 8% were alcoholics (n=2) .

The above said are depicted diagrammatically in table no: 1

Table No. 1

Co-morbid disease	Number of patients	percentage
DM	8	32%
Smokers	4	16%
Serious systemic disease	2	8%
Alcoholics	2	8%

All the 9 randomized participants and 3 healthy volunteer underwent baseline testing . No adverse effects were reported during the treatment period . Additional details on participants recruitment and retention are provided in table no : 2



DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

The demographic and clinical characteristics of each group are shown in table No: 3

Table No: 3

Particulars	Normal control (n =3)	Group 1 (n =3)	Group 11 (n =3)	Group 111 (n =3)
Supplement				
• Folic acid		+	+	+
• Methylcobalamine			+	+
• Pyridoxine				+
Age (year)	40 \pm 9	43 \pm 9	53 \pm 5	55 \pm 9
Male : female	2:1	2:1	2:1	2:1
Serumcreatinine (mg /dl)	0.7 \pm 0.1	7 \pm 2.4	4.3 \pm 2.1	4.1 \pm 1.4
Haematocrit (%)	31 \pm 2.4	24.1 \pm 2.7	29.1 \pm 2	27 \pm 1.9

Treatment effect on total homocysteine (tHCY) in cardiovascular disease

Table No. 4

Group	Mean fasting total Homocysteine Before treatment (mmol/L)	Mean fasting total Homocysteine After treatment (mmol/L)	Mean reduction Total homocysteine by treatment (mmol /L)
1	17.6	13.8	3.8
11	18.2	11.4	6.7
111	17.9	10.4	7.1

After administration of folic acid to group 1 , results in mean reduction of total homocysteine level of 3.8 mmol/L, folic acid and methylcobalamine to group 11 results in mean reduction of total homocysteine level of 6.7 mmol/L , and to group 111 by co administration of folic acid, methylcobalamine and pyridoxine results in significant mean Reduction of total homocysteine level of 7.1mmol/L implies the significance of folic acid , methylcobalamine , pyridoxine as homocysteine lowering vitamins.

DISCUSSION

From our study we should make a special not a fact that high homocysteine levels in CVD patients, which has proven quite refractory to pharmacological doses of folic acid supplementation is significantly reduced by co-administration methylcobalamine and pyridoxine. this method of therapy for hyperhomocysteinemia could combat the risk of CVD. Folate in the form of 5- MTHF, donates a methyl group in the remethylation of homocysteine to methionine. folic acid is a stable form of folate , which is rapidly converted to active forms in in-vivo. administration in daily doses of 5mg will consistently lower the homocysteine

plasma concentration by 25% in normal subjects. smaller doses(100 – 400mg/dl)appear to be almost as effective and fall with in the range that can be modified by nutritional interventions such as food fortification. hence, folic acid offers the prospect of an effective safe and economical therapy for hyperhomocysteine.

Administration of methylcobalamine, which is co-enzyme in methionine remethylation pathway was anticipated to be another strategy to cure hyperhomocysteinemia. Our study indicates that administering folic acid along with methylcobalamine and pyridoxine are for the homocysteine levels to reach normal.

Our study suggest that supplementation of folic acid along with methylcobalamine and pyridoxine are essential for the remethylation pathway to regain its normal activity. this treatment for hyperhomocysteinemia in cardiovascular disease could be a therapeutic strategy to combat the risk associated with homocysteine levels in cardiovascular disease patients.

CONCLUSION

The prospective randomized study of homocysteine lowering vitamin in severe cardiovascular disease patients provides considerable evidence that hyperhomocysteinemia is strongly and independently related to vascular disease including atherosclerosis , carotid artery venous thrombosis, MI, stroke.

Our study supports that the co-administration of folic acid , methylcobalamine ,pyridoxine as homocysteine lowering vitamins in cardiovascular disease . lowering serum concentration of homocysteine has been proven to reduce the risk of adverse cardiovascular events among peoples , but studies have not yet proven whether lowering homosysteine levels reduce the incidents of heart attacks or strokes among people with mild elevated levels of homocysteine.

Screening for elevated homocysteine levels is advisable for individuals who manifest coronary artery disease, that is out of proportion of their traditional risk factors or who have a family history of premature atherosclerotic disease.

Elevated homocysteine levels can be caused by vitamin B12 deficiency due to impaired absorption of vitamin B12 caused by gastric atrophy. Vitamin B12 deficiency leads to anemia and, if not corrected in time permanently damage the nervous system. folic acid supplements will correct the anemia but they do not prevent the damage . for this reason , people over the

age of 50 years, who taking folic acid supplements should also take at least 25mcg of vitamin B12 and 10mg vitamin B6 per day.

Reducing homocysteine doses not quickly repair existing damage of the artery architecture . the main role of reducing homocysteine is likely in PREVENTION But with a slow but probable role in CURE.

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