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BARRENNESS



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HYPERHOMOCYSTEINEMIA



Homocysteine is a sulphur containing amino acid that is closely related to the essential amino acids methionine and cysteine .

Homocysteine cycle:

Three steps are involved in Homocysteine cycle:

1. Homocysteine is converted to methionine due to methyl group donation from methylcobalmine.
2. Pyridoxine (VitaminB6) helps in conversion of homocysteine to cysteine
3. Folic acid helps in remethylation process. In a nutshell for maintaining normal homocysteine levels folic acid, methylcobalamine and pyridoxine play important role.

Consequence of Hyperhomocysteinemia are as under:

1.Elevated plasma homocysteine concentration could cause atherosclerosis and some brand homocysteine as new cholesterol or cholesterol of the 90 th century. Hyperhomocysteinemia can also lead to hypertension since homocysteine generates oxygen radicals such as superoxide anion and hydrogen peroxide that are known to produce Vasoconstriction. It is possible that hypertension in diabetic patients may be due to increased levels of plasma homocysteine. It is also possible that hyperhomocysteinemia may be involved in induction and sustaining hypertension in diabetic patient. In another study on homocysteine and hypertension , it has been mentioned that elevated homocysteine diminishes the vasodilation by nitric oxide , increases oxidative stress vasodilation by nitric oxide , increases oxidative stress, stimulates the proliferation of vascular smooth muscle cells, and alters the elastic properties of the vascular wall.[1]

2.Elevated plasma homocysteine is attributed in causing endothelial injury ,increased production of platelet aggregating factor, such as thromboxane A2 and also inhibition of natural anticoagulation pathway. In another study it was suggested that hyperhomocysteinemia is possible casual factor in free radical generation during acute phase of thrombotic cerebrovascular stroke.

3.Coronary artery disease (CAD) : Hyperhomocysteinemia is branded as hottest risk factor for stroke and heart disease including Acute Heart Attack. A group of workers reported

elevated plasma homocysteine and increased mortality in patients with coronary artery disease.[2] in another prospective cohort study suggested intake of folate and Vit. B6 (pyridoxine) in the primary prevention of coronary artery disease among women.[3] In another study authors suggested elevation of homocysteine in all young patients of coronary artery disease in the absence of traditional risk factors.[4]

4. Peripheral Arterial Disease (PAD)- It also includes carotid artery stenosis. High plasma homocysteine increases platelet aggregation, oxidative stress, vascular smooth muscle proliferation, decrease nitric oxide production and impairs endothelial function. Hyperhomocysteinemia induces atherosclerosis and a prognostic indicator of cardiovascular morbidity and mortality in Peripheral Arterial Disease.[5] Likewise in another study , it has been observed if a relation between the maximum degree of stenosis of extracranial carotid arteries and plasma homocysteine concentration as well as plasma concentration and intakes of vitamins involved in homocysteine metabolism. The result suggested high plasma homocysteine concentration and low concentration of these vitamins in production of coronary artery stenosis.[6]

5. Strokes and Cerebral Venous Thrombosis- In various studies conducted reported elevated levels of homocysteine in patient with stroke and transient ischemic attack and also one of the risk factors for hip fractures in stroke patients.[7] It has been suggested that total homocysteine concentration is a strong predictor for incidence of ischaemic stroke among patients at increased risk because of chronic coronary heart disease.[8]

6. Impaired cognitions and alzheimers disease (AD) and other Neurodegenerative disorder including Parkinsons disease-

Recently poor cognition joined the list of adverse effect of hyper homocysteinemia. Elevated homocysteine is a marker indicating risk factor for both vascular dementia alzheimers disease.[9] Elevated homocysteine was associated with decreased cognition in subjects older than 65 years.

Several studies have shown the existence of a correlation between cognitive skills and the serum concentrations of homocysteine and vitamins involved in homocysteine metabolism.[10] In another study it was found that elevated level of homocysteine markedly increases the vulnerability of hippocampal neurons to excitotoxic and oxidative injury in cell culture and in vivo suggesting a mechanism by which homocysteine may contribute to pathogenesis of neuro degenerative disorder.

Another study suggested reduction in homocysteine levels in healthy older people, may help to prevent Alzheimer□s disease. In Parkinsons disease elevated levels

of homocysteine is associated because levodopa metabolism produces homocysteine, the extent of which is B vitamin status. It is observed that elevated plasma homocysteine level is associated with an increased risk of vascular and degenerative dementia.

7. Schizophrenia- Plasma homocysteine levels were measured in patient with chronic schizophrenia which was found markedly elevated as compared to healthy subjects. Similarly elevated levels of homocysteine in young male patients with schizophrenia could be related to the patho-physiology of Schizophrenia.[11]

Conclusion- Homocysteine is among the hottest risk factors for stroke and heart attack. A person may have low cholesterol level; low blood pressure may die of a heart attack due to hyperhomocysteinemia.

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Relationship between chemical structure of Homocysteine and Methionine

HS-S-CH1-CH1-CHNH1 C=O-OH---------H1C-S-CH1-CH1-CH-NH1-C==O-OH

Homocysteine Methionine

Homocysteine cycle

Remethylation

Tetrahydrofolate

5,10- methylene tetrahydrofolate Methyl B12

5, Methyltetrahydrofolate

Proteins

Methionine

Dimethylglycine

Betaine

Homocysteine+B6

Cystathionine

Cysteine

Transulfuration

Transmethylation

S-Adenosylmethione

S-Adenosylhomocysteine

1. Methionine Synthase

2. 5,10-methylene tetrahydrofolate reductase

3. Betaine homocysteine methyltransferase

4. Cystathionine beta-synthase.

Dr. Sanjay Agrawal,
Leading Pharmaceutical Consultant and Editor-in Chief of IJM Today
Post Graduation Diploma in Naturopathy and Yoga,
6/146, Malviya Nagar,
Jaipur -302017 ,
Rajasthan