

Issue 104

In a nutshell

New studies have refined our understanding of the impact of elevated homocysteine on cardiovascular disease.

Venous thrombosis is one condition linked with low Hcy. Patients with bowel disease (e.g. IBD or short bowel) are at greater risk. Those with a genetic mutation involving Hcy metabolism are another group.

Homocysteine and venous thrombosis

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NUTRITION RESEARCH REVIEW

Study one: Venous thrombosis in short bowel syndrome

Venous thrombosis in patients with short bowel syndrome is related to hyperhomocystinemia, according to recent American research.

Researchers studied 17 patients with short bowel syndrome. Ten of these patients had evidence of venous thromboses, based on venogram and ultrasound.

There was a significant correlation between number of venous thromboses in each patient and their homocysteine levels (relative risk of venous thrombosis for highest vs lowest tertile of total Hcy =3.6, 95% CI 1.88-5.34, p was <0.01).

None of the patients had abnormal vitamin B12 or folate levels, although in 7 patients an abnormal status was suggested by higher than normal methylmalonic acid level along with elevated total Hcy.

Reference: Compher CW et al. Hyperhomocysteinemia is associated with venous thrombosis in patients with short bowel syndrome. J Parenter Enteral Nutr 2001;25:1-7

Study two: Venous thrombosis in inflammatory bowel disease

Elevated homocysteine (Hcy) levels are often seen in inflammatory bowel disease (IBD), but do not seem to be related to the higher incidence of venous thrombosis, according to a study from Holland.

Subjects: 231 consecutive patients with IBD and 102 healthy controls of similar age and gender. A history of venous thrombosis was seen in 7% and of arterial

thrombosis in 4% of these patients.

Method: Case-control retrospective study.

Results: Hcy levels were correlated with those of serum folate, vitamin B₁₂ and pyridoxine. The IBD patients had a higher prevalence of elevated total Hcy than controls (11% vs 5%, p = 0.07) as well as higher mean Hcy levels. However, the Hcy levels were not significantly different in those patients with a history of thrombosis than those without.

Reference: Oldenburg B. et al. Homocysteine in inflammatory bowel disease: a risk factor for thromboembolic complications? Am J Gastroenterol 2000;95:2825-30

Study three: Genetic mutation affects homocysteine levels

Patients with venous thrombosis and elevated homocysteine levels may well have a genetic mutation, but will still respond to folate supplementation. These are the conclusions from a recent Italian study.

Subjects: 170 consecutive patients with documented early-onset thrombosis (venous and arterial, mean age of subjects 41 years) and 182 age and gender matched controls.

Method: Case-control study. The mutation studied was the one involving substitution of a C-T base pair in the gene for the enzyme methylenetetrahydrofolate reductase, which is involved in Hcy metabolism. Subjects with elevated homocysteine were given folate supplementation.

Results: Patients were significantly more likely to have elevated Hcy than controls (odds ratio= 3.25, 95% confidence interval 1.78-5.91), but not more likely to have deficient folate or B₁₂.

Both patients and controls had approximately the same frequency of the mutation (28% vs 22%). The relationship between Hcy and folate/B₁₂ levels (negative correlation) was greater in those with the

mutation than in those without it. However, even in those subjects elevated Hcy levels returned to normal after folate supplementation.

Reference: D'Angelo A. et al. The role of vitamin B12 in fasting hyperhomocysteinemia and its interaction with the homozygous C677T mutation of the methylenetetrahydrofolate reductase (MTHFR) gene. A case-control study of patients with early-onset thrombotic events. Thromb Haemost 2000;83:563-70

Comments

It has been known for some time that an elevated homocysteine level is an independent risk factor for ischaemic cardiovascular disease. Recent clinical research has tended to focus on more specific situations.

One example is the role of elevated Hcy levels in venous thrombosis. A number of epidemiological studies have shown that there is a correlation between the two. It may be possible that lowering Hcy levels through supplementation and diet will help prevent venous thrombosis in high risk patients.

One such group are patients with gastrointestinal diseases such as inflammatory bowel disease and short bowel syndrome. These patients are known to be more susceptible to venous thromboses. This can be a particularly serious problem when they require parenteral nutrition support, because thromboses can occur around catheter lines. Patients with such GIT diseases are also more likely to have nutritional deficiencies which might elevate Hcy, such as lack of folate and vitamin B₁₂.

Hence the value of the first two studies summarised in this issue. They confirm that elevated Hcy is indeed likely to be seen in IBD and short bowel syndrome, though only the first study suggests that this in turn is

correlated with venous thrombosis.

At the same time, they confirm what a number of other studies have shown - that a patient with elevated Hcy does not necessarily also have an obviously abnormal level of serum folate or vitamin B₁₂.

Even without an obviously deficiency, the balance of research shows that increasing the intake of folate and vitamin B₁₂ usually lowers elevated Hcy levels. What we are still lacking to date are randomised trials showing whether this in turn has any impact on clinical outcomes - in this case the rate of venous thrombosis.

The third study confirms what other studies have shown - that humans have a common mutation of a key enzyme involved in the metabolism of homocysteine and that people with this mutation seem to have a greater need for folate and vitamin B₁₂. It also shows that this mutation should not prevent the correction of the elevated Hcy through supplementation or diet.

In conditions where levels of these nutrients are low or borderline, people with this mutation seem to be more likely to become hyperhomocysteinaemic. Is it worth testing patients with elevated Hcy for this genotype? It is still too early to know.

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