Association of homocysteinaemia with hyperglycaemia, dyslipidaemia, hypertension and obesity

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Abstract

Aim: Hyperhomocysteinaemia and the metabolic syndrome are associated with increased cardiovascular risk. We investigated whether there is a link between the metabolic syndrome or its components and homocysteine levels in a population without cardiovascular disease.

Methods: From the population sample of 382 participants (286 females and 96 males) we isolated those reflecting the metabolic syndrome and determined their homocysteine levels. We then evaluated the association of homocysteine with hyperglycaemia, hypertriglyceridaemia, hypercholesterolaemia, hypertension and obesity, using a significance level of \( p = 0.05 \). Enzymatic methods were used for all biochemical parameters.

Results: We found the statistical relationship between homocysteine and the metabolic syndrome as follows: hyperglycaemia (\( p = 0.175 \)), hypertriglyceridaemia (\( p = 0.442 \)), hypercholesterolaemia (\( p = 0.480 \)), obesity (\( p = 0.080 \)); and hypertension: systolic pressure (\( p = 0.002 \)) and diastolic pressure (\( p = 0.033 \)).

Conclusion: We found no statistically significant association between baseline plasma homocysteine levels and the metabolic syndrome, except for hypertension.

Keywords: hyperglycaemia, hypertriglyceridaemia, hypercholesterolaemia, hypertension, obesity, homocysteine

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Diabetes mellitus is a group of metabolic diseases characterised by hyperglycaemia, resulting from defects in insulin secretion, insulin action or both. It is associated with several cardiovascular disorders, including angioptathy and platelet hyperactivity, which are major causes of morbidity and mortality in type 2 diabetes mellitus. Atherosclerosis is substantially more prevalent and progresses rapidly in diabetes mellitus. There are an estimated 23.6 million people in the USA (7.8% of the population) with diabetes. The vascular complication of diabetes mellitus, at its earliest stage, is manifested as endothelial dysfunction, decreasing the bioavailability of nitric oxide, which protects blood vessels from endogenous injuries. Hyperglycaemia inhibits fibrinolysis by decreasing the activity of plasminogen activator and enhances coagulation by activating procoagulants into thrombosis.

Homocysteine is an amino acid derived from methionine. The latter is an intermediate in the conversion of homocysteine to cysteine. Homocysteine is metabolised via two pathways: remethylation, in which homocysteine is converted into methionine, and transulfuration, in which homocysteine is converted into cysteine. In the former pathway, homocysteine acquires a methyl group, either from the conversion of 5-methyltetrahydrofolate into hydrofolate or from the conversion of betaine into the N' N-dimethylglycine. Vitamins B6, B12, and folic acid are important in the conversion of 5-methyltetrahydrofolate into hydrofolate and therefore for the remethylation pathway and the metabolism of homocysteine into methionine.

Epidemiological studies suggest hyperhomocysteinaemia to be an independent risk factor for developing atherothrombosis vascular disease. Mechanisms by which hyperhomocysteinaemia causes vascular disease include promotion of atherosclerosis by damaging the inner lining of arteries and promoting thrombosis through pathological collagen activation of the intrinsic pathway, impairment of thrombolysis, increased production of hydrogen peroxide, endothelial dysfunction, and increased oxidation of low-density lipoproteins.

Some of the complications of arterial thrombosis following hyperhomocysteinaemia include coronary heart disease, myocardial infarction, stroke, peripheral vascular disease, miscarriage, pulmonary embolism, retinal embolism and neural tube defect (spina bifida). The homocysteine level may be increased in hypertensive, overweight and obese subjects. Homocysteine is thought to help regulate glucose metabolism and insulin absorption. Homocysteine has been suggested to contribute to the atherosclerotic process of diabetes mellitus. High homocysteine levels have been reported in diabetic patients, and elevated levels are a strong risk factor in these patients. The elevation occurs particularly in patients with type 2 diabetes, as well as in individuals in prediabetic states who exhibit insulin resistance. The levels of homocysteine in such individuals are also influenced by their insulin concentrations, and therapy with insulin and medications such as metformin and glitazones that can either raise or lower homocysteine levels.

The effect of hyperhomocysteinaemia on diabetes and insulin resistance has been reported with unclear synergism. Homocysteine levels have been reported as either low or elevated compared to non-diabetic subjects, reflecting the potential role of homocysteine in the development of macro- and microvascular disease in diabetic patients. Shaikh et al. found that 58% of their diabetic participants had elevated homocysteine levels and males were predominant in this group. This finding is consistent with that of Schalinske’s study.

These authors reported a strong association between atherosclerosis, hyperhomocysteinaemia and type 2 diabetes mellitus.