

Research Article

Hyperhomocysteinemi in Patients with Diverticula of the Colon

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Abstract

Objectives: Hyperhomocysteinemia (HHcy) have been associated with cerebrovascular events, cardiac diseases and vascular thrombosis. HHcy is caused by cyanocobalamin and folate deficiencies. Diverticula of the colon (DC) is caused by herniation of the colonic mucosa and submucosa. The aim of this study was to evaluate serum homocysteine levels in patients with DC.

Methods: We consecutively evaluated 115 patients (65 male, mean age 65±12.1 years) with DC. Baseline serum levels of homocystein, folate and vitamin B12 were retrospectively obtained from hospital data. Plasma homocystein was measured by high performance liquid chromatography with a fluorescence detector. Diagnosis of DC was done by colonoscopy. The chi-squared test and independentt test were used for comparison.

Results: DC patients had significantly higher levels of homocysteine compared with normal levels (16.4±11.2 µg/l; normal ranges 0-12 µg/l). Otherhand, mean vitamin B12 level was 470±317mg/dl and theme an folate level was 9.3±4.3 mg/dl. According to multiple logistic regression, HHcy developed more with aging and male gender was a strong risk factor for HHcy (all p<0.001).

Conclusion: Screening for HHcy should be recommended in subjects with DC. HHcy could also lead to DC. Particularly, elderly male patients with DC should be treated with folate and cyanocobalamin if laboratory data indicates features of HHcy.

Keywords: Colon, diverticula, hyperhomocysteinemia

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DC is associated with increased healthcare burden and cost in worldwide. The diagnosis of DC relies both on colonoscopy and computed tomography of abdomen. The prevalence of DC is also increasing at an alarming rate, especially in the elderly population. It is estimated that at least 25 percent of subjects above than 50 years have DC.^[1]

A recent population-based Danish study showed that DC

was dominantly accumulated among some families suggesting genetic factors were closely linked to risk of DC.^[2]

On the other hand, authors showed that low fiber intake was not associated with an increased risk of diverticulosis.^[3]

Homocysteine (Hcy) is a sulfur-containing amino acid that is generated during methionine cyclus. Driving factors of hyperhomocysteinemia (HHcy) are mostly due to deficien-

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cy of either vitamin B12 or folate. HHcy may cause an increased risk for cardiovascular and intracranial events.^[4]

Several studies have shown that IBD patients have a increased risk for HHcy compared to healthy counterparts and administration of Hcy is responsible for alleviation of IBD via accumulation of cell adhesion molecules entire the colonic mucosa.^[5, 6]

Currently clinical guidelines never recommend screening HHcy in patients with DC primarily because of the limited data on the effect of HHcy on the disease, and the lack of studies evaluating the impact of hyperhomocysteinemia on the risk of DC. There are no data on the incidence of HHcy in patients with DC.

Methods

This retrospective study included 115 patients with DC at a large tertiary care hospital between July 2018 and December 2018. Demographic, laboratory, and clinical data including serum homocysteine levels was abstracted the time of enrollment. The mean age was 65±12.1 years and 55 % were male. Baseline concentrations of serum levels of Hcy, folate and vitamin B12 were retrospectively obtained from hospital data. Serum homocysteine levels were obtained from only 18 patients. Serum homocysteine concentration was measured by high performance liquid chromatography with a fluorescence detector. Diagnosis

of DC was done by colonoscopy. The chi-squared test and independent t test were used for comparison (Table 1).

Results

DC patients had significantly higher levels of homocystein compared with normal levels (16.4±11.2 µg/l; normal ranges 0-12 µg/l). There was mild HHcy among patients with DC. Otherhand, mean vitamin B12 level was 470±317 and the mean folate level was 9.3±4.3. There was no deficiency involving both vitamin B12 and folate levels among study population. According to multiple logistic regression, HHcy developed more with aging and male gender was a strong risk factor for HHcy (all p<0.001). Other factors independently associated with HHcy were age (HR 1.05), DM (HR 1.55) WBC (HR 1.0) and serum folate levels (HR 1.12).

Discussion

In this small restospective study of 115 participants, we discovered that subjects with DC were characterized by a higher homocystein levels, probably secondary to low fiber diet-related HHcy. This causal relationship has been revealed at the first time in the English literature.

Diverticular disease of the colon DC is pouches of the colonic wall into peritoneum and it is the sixth most common outpatient gastrointestinal diagnosis in the western world particularly in the USA.^[7]

Table 1. Baseline characteristics of the study patients

	n	Minimum	Maximum	Mean	SD
Age (year)	115	27.00	94.00	65.0180	12.16675
Hemoglobin (g/dl)	115	8.30	15.90	12.9612	1.70171
Hematocrit (%)	115	27.10	49.00	39.8236	4.72380
MCV (fL)	115	65.60	124.20	87.2018	7.62225
WBC (mm ³)	115	2.89	31.30	7.1344	2.69576
Platelet (109/L)	115	52.00	529.00	245.2667	68.10350
Glucose (mg/dl)	115	73.00	318.00	118.6250	47.17914
Urea (mg/dl)	115	15.00	254.00	39.5370	29.06752
Creatinine (mg/dl)	115	.42	8.27	.9664	.71707
AST (U/L)	115	7.00	350.00	23.8662	28.22735
ALT (U/L)	115	6.00	71.00	20.9814	12.17142
Total proteine (g/dl)	115	5.50	8.76	7.2781	.48404
Albumin (g/dl)	115	1.80	5.30	4.6541	.41393
Neutrophil (%)	115	2.01	9.80	4.2136	1.47599
Calcium (mg/dl)	115	7.80	10.94	9.6550	.46470
Homocysteine (µg/l)	18	9	43	16.42	11.218
Folate (ng/ml)	94	3.100	20.000	9.36840	4.362582
Vitamin B12 (pmol/L)	115	178.200	2000.000	470.42922	317.867999
Valid N (listwise)					

MCV: Mean corpuscular volume; WBC: White blood cell counts; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; SD: Standard deviation.

Homocysteine is a key step inside one-carbon metabolism and remethylation. A recent Chinese metaanalysis has showed that approximately 5 $\mu\text{mol/L}$ increase in serum homocysteine levels increased the incidence of digestive tract cancer by 7%.^[8]

A Korean study involving 1039 subjects who underwent a colonoscopy and plasma homocysteine concentration determination during health examinations at single center over a two-year period showed that HHcy was a risk factor for colorectal adenoma in women.^[9]

It has been also a well-known fact that younger age, lower fibre and higher carbohydrate intakes were associated with lower blood folate as well as higher homocysteine levels.^[10]

A British cohort also showed that high folate intake was strongly related to high intakes of vegetables, fruit and low fibre breakfast cereal, and low intakes of processed meat, white bread, sugar and preserves.^[11]

We concluded that increased awareness of screening for serum homocystein levels is needed in patients with DC. This phenomenon may have been related to dietary factors that causes both HHcy and DC.

On the otherhand, an animal study to explore the effect HHcy on colon transit time and its role in intestinal remodeling has showed that intestinal motility was decreased in HHcy due to matrix metalloproteinase-9 (MMP-9) induced intestinal remodeling. This striking effect of HHcy has resulted in decreased intestinal motility and constipation in high methionine diet-fed rats.^[12]

We concluded that decreased bowel motility (constipation) during HHcy was also a contributing factor to develop DC in human.

There were several limitations of the study. First, study findings may not be generalized entire the subjects with DC due to small sample size. Second, there was not a control group amid retrospective nature of the study. Third, we did not obtain dietary behaviours of the subjects with DC which causes HHcy. On the otherhand, we found a robust association between HHcy and DC in which other authors never conducted a study like this.

Conclusion

Patients with DC are at increased risk of hyperhomocysteinemia. Prompt recognition of HHcy in such patients might prevent possible stroke and intravascular thrombus and reduce the risk of in-hospital mortality in DC. This is the first systematic study to examine the rate of HHcy in DC patients. Treatment with cyanocobalamine and folate may reduce the risk of thromboembolic events in patients with DC particularly who treated in intensive care units.

Disclosures

Ethics Committee Approval: The study was approved by Ilhan Ozdemir Research And Training Hospital (Date: 15.02.2019/ number: 85554271-000-1614).

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