Sys Rev Pharm 2020; 11(2): 454 – 457
A multifaceted review journal in the field of pharmacy
E-ISSN 0976-2779 P-ISSN 0975-8453

Relationship between Blood Homocystein Level and Acute Stroke in Patients of Al-Muthanna Province\Iraq

Asaad Adil Mnaather[1], Haider Ali Hussien[2], Ali Abdulkarim Talib[3]
Al-Muthanna University, College of Medicine, Department of Medicine M.B.Ch.B., F.I.CM.S[1]
Al-Muthanna University, College of Medicine, Department of Medicine M.B.Ch.B., F.I.CM.S[2]
Al-Muthanna University, College of Medicine, Department of Medicine M.B.Ch.B., F.I.CM.S[3]
Corresponding author: Department of Medicine, College of Medicine, Al-Muthanna University, Iraq.
E-mail: asaadneuro@yahoo.com asaadneuro@mu.edu.iq

Article History: *Submitted: 23.11.2019* *Revised: 20.01.2020* *Accepted: 24.02.2020*

ABSTRACT

Background and purpose: Homocysteine is a toxic, sulfur-containing intermediate of methionine metabolism. Elevated blood homocystein, as a result from a consequence of impair metabolism or defect in co-factors that participate in recycling, regarded as independent risk factors for stroke. The goal of this study to measure blood homocystein level within 24 hours from acute stroke and its relation with recurrence also to compare homocystein levels between ischemic and hemorrhagic stroke.

Methods: this study was a cross-sectional hospital-based study, done from July(2019) –January(2020) consisting of 100 Iraqi acute stroke patients whose are selected randomly from neurological ward in AL-Muthanna teaching hospital, on patients aged (50-80)years. Fasting homocystein level assessed within 24 hours after acute stroke.

Results: Male:Female ratio 1.2:1 and mean age 64.7±11.699. The mean total plasma homocystein level was (20±6.2), the total plasma homocystein level was significantly elevated in ischemic stroke patients (P value <0.0001) than hemorrhagic or TIA stroke types. Recurrent stroke was mostly prevalent in those with intermediate total plasma homocystein (90.9%) while (9.1%) of those had moderate homocystein level.

Conclusion: this study confirmed that elevated homocystein level regard as independent risk factors for stroke and important factor for recurrent stroke that need to be involved in secondary stroke prevention.

Key word: Homocystein, Cerebral infarction, recurrent stroke and risk factor

Correspondence:
Asaad Adil Mnaather
Al – Muthanna University
College of Medicine
Department of Medicine
Iraq
E-mail: asaadneuro@yahoo.com

DOI: 10.5530/srp.2020.2.68

INTRODUCTION

Identification of modifiable risk factors for stroke is important in secondary prevention from recurrent of stroke and from other vascular event. Some studies regard increased blood level of homocystein is one of the modifiable risk factor for recurrent stroke .[1-6] prospective studies with assessment of total serum homocystein level before vascular events is more informative than obtained later on because many disease can effect on homocystein readings. [7] The British Regional Heart Study,[14] show there is correlation between total homocystein value and recurrence of stroke and other vascular events.

Homocystein is produced from essential amino acid called methionine by process of demethylation. Homocystein is metabolized by either remathylation or transmathylation [8]

So there is other causes of homocystein deficiency like congenital deficiency in enzymes that is needed for metabolism of homocystein and lead to elevated level of homocystein in blood that can contribute to arterial damage and blood clots in blood vessels. Coffee consumption, smoking, renal failure and types of drugs can also effect serum level of homocystein.[8]

This study involved measurement the blood homocystein level at morning afterward admittance of patients diagnosed TIA, ischemic stroke as well as ICH.

METHODOLOGY

1. Patients and methods

This cross sectional study, consisted of 100 patients in Al-Hussein teaching Hospital in Al-Muthanna province\Iraq who had been selected randomly after acute onset of cerebrovascular events from July 1, 2018 to January 8, 2020. Those patients diagnosed by assessment of clinical feature depend on National Institute Of Health Stroke Scale (NIHSS) [9] to assess the severity of stroke and using Computed Topography (CT) scan. So ischemic stroke diagnosed if the clinical feature presumed more than (24hours) and CT scan show evidence of early infarction in distribution of cerebral arterial territories. TIA had same feature of acute ischemic stroke but CT scan was normal and duration is less than 24 hours while ICH diagnosis depend mainly on CT scan to detect it.

Baseline data like age, gender, Diabetes mellitus, Hypertension and smoking all was included in Questionnaire list. History of TIA or stroke was registered by depending on self –reported or from medical card records in hospitals.

Total homocystein level was done for those stroke patients with routine workup. After fasting overnight, total homocystein level was assessed in morning soon after admittance within about 24 hrs. Later stroke start. The blood sample is kept freezing until centrifuged by using For the analysis, Abbott's automated immunofluorescence homocystein test (Abbott ImX method, Abbott Laboratories).Normal level of the serum homocystein is below 15 mcmol\L, so higher level of homocystein classified into three categories[10]

Normal value	Moderate elevation	Intermediate elevation	Sever Intermediate
<15 mcmol\L	15-30 mcmol/L	30-100 mcmol/L	100 mcmol/L>

Stoke patient are treated regularly in neurological ward according to guideline .when the measured total serum homocystein level >15 mmole, this elevated value, so need to give advice to patients after discharge regarding his diet or supplement with folic acid.

2. Statistical analysis:

All continuous data follow a normal distribution, so mean and standard deviation was used to represent the data. The total plasma homocystein level were presented as charts and tables in simple proportion and comparisons of subgroups were done by using Pearson Chi-square test. Data of the research was analyzed by using SPSS version 23. The statistical significant difference for p-value less than 0.05 was taken at confidence interval of 95%

Objective of study: The aim of study to determine that total plasma homocystein is independent risk factors for stroke and its relation to recurrent stroke.

RESULTS

A cross sectional hospital based-study was conducted on 100 patients with acute stroke and measured total homocystein level for them. Male:Female ratio 1.2:1 and mean age 64.7±11.699. The mean total plasma homocystein level was (20±6.2). It showing that moderate plasma homocystein level was mostly seen in stroke patients.

Higher percentage of moderate plasma homocystein level was in those with TIA (88.2%), then in those with ischemic stroke (84.3%) and only (7.7%) in those with hemorrhagic, and this association was statistically highly significant.

Table 1- Relationship plasma homocystein level and prevalence of CT-based stroke patients

Total plasma homocystein	CT-based stroke type			Total	Fisher exact test ,P value
	hemorrhage	Ischemia	TIA		
intermediate	0 0.0%	10 14.3%	0 0.0%	10 10.0%	
moderate	1 7.7%	59 84.3%	15 88.2%	75 75.0%	
normal	12 92.3%	1 1.4%	2 11.8%	15 15.0%	
Total	13 100.0%	70 100.0%	17 100.0%	100 100.0%	59.163 , 0.0001

Recurrent stroke was mostly prevalent in those with intermediate total plasma homocystein (90.9%) while (9.1%) of those had moderate homocystein level, and this association was statistically highly significant.

Table 2: Relationship between total plasma homocystein and recurrent stroke

Stroke	Elevation of homocysteine test			Total	Fisher exact test, p-value
	intermediate	moderate	normal		
Not Recurrent	0 0.0%	74 83.1%	15 16.9%	89 100.0%	
Recurrent	10 90.9%	1 9.1%	0 0.0%	11 100.0%	
Total	10 10.0%	75 75.0%	15 15.0%	100 100.0%	58.681, 0.0001

DISCUSSION

This study included 100 acute stroke patients that attend Al-Muthanna hospital\Iraq with Male:Female ratio 1.2:1 and mean age 64.7±11.699. The mean total plasma homocystein level was (20±6.2).

This study show elevated total serum homocystein level for acute ischemic stroke patients and can regarded this as independent risk factors for recurrent stroke and this result are in agreement with a results of [11] who found that total homocystein was above the 75th percent in those with recurrent ischemic stroke and others vascular. But in this study is mainly focusing on total homocystein as risk factors for recurrent stroke.

Also the strength of this study that make it difference from others that it show significant differences between an ischemic and the hemorrhagic stroke. This difference mean that elevated level of total homocystein in ischemic stroke is not just a reactionary effect to stroke but can be explained by different vascular pathology between ischemic and hemorrhagic stroke. While [12] and [22] found that no difference in total homocystein value between patients with cerebral infarcts and those with ICH because in their study, the number of intracranial hemorrhage was less.

This study show elevated total plasma homocystein is significantly occur with recurrent ischemic stroke and that is agree with comparable to result of [12] Some researchers had find correlation between hyper-homocystenemia and ischemic stroke and its subtype. [12–15] [13] found that total homocystein level was so elevated in patients with complete middle cerebral artery infarct group than other subtypes which can be due to study done on higher age group patients.

Eikelboom et al[14]was found significantly elevated blood homocystein level of arterial occlusion (large or small arteries) in compared with healthy control people. While Tan et al[15] that his study found higher total serum homocystein value in large-artery infarction as comparing with a small-artery strokes in patients.

But the question is still present ,whether hyper-homocystenemia is risk factor for stroke or only vascular marker? .Many study like McCully KS et al,[16] supported that is increased homocystein value is risk factor for stroke by observation that hyper-homocystenemia due to deficiency in one of the following enzymes (methylenetetrahydrofolate reductase , MTHF homocysteine methyl transferase , cystathionine synthase) is the causes of serious vascular events[3,17,18,19]. Also in many neurological disorders, injury to neurons is mainly by overstimulation by excitatory amino acid like aspartic acid and glutamic acid that can be activated by hyper-homocystenemia.

So all of the above mention theory support the pathogenesis of hyper-homocystenemia and that elevated total homocystein is independent risk factors for recurrent stroke.[20]

CONCLUSION

The present data suggest that elevated total homocystein is an independent risk factor for recurrent stroke. Evaluation of homocystein may become a part of the routine workup of stroke patients. Elevated homocystein values may easily be reduced by vitamin replacement, and this is important in planning for secondary stroke prevention.

Recommendation

Further studies were needed to more clarifying relationship between homocystein and stroke, also to explained whether treating hyper-homocystenemia can reduced the stroke in future.

REFERENCES

1. McCully KS. Homocysteine and vascular disease. *Nat Med*. 1996;2: 386–389.
2. Malinow MR. Homocyst(e)ine and arterial occlusive diseases. *J Int Med*.1994;236:603–617.
3. Selhub J, Jacques PF, Bostom, D'Agostino RB, Wilson PWF, Belanger AJ, O'Leary DH, Wolf PA, Schaefer EJ, Rosenberg IH. Association between plasma homocysteine concentrations and extracranial carotidartery stenosis. *N Engl J Med*. 1995;332:286–291.
4. Brattström L, Lindgren A, Israelsson B, Andersson A, Hultberg B. Homocysteine and cysteine: determinants of plasma levels in middle-aged and elderly subjects. *J Intern Med*. 1994;236:633–641.
5. Graham IM, Daly LE, Refsum HM, Robinson K, Brattström LE, Ueland PM, et al. Plasma homocysteine as a risk factor for vascular disease: the European Concerted Action Project. *JAMA*. 1997;277:1775–1781.
6. Kittner SJ, Giles WH, Macko RF, Hebel JR, Wozniak MA, Wityk RJ, Stolley PD, Stern BJ, Sloan MA, Sherwin R, et al. Homocyst(e)ine and risk of cerebral infarction in a biracial population: the Stroke Prevention in Young Women Study. *Stroke*. 1999;30:1554–1560.
7. Aronow WS. Ahn C, Gutstein H. Increased plasma homocysteine is an independent predictor of new atherothrombotic brain infarction in older persons. *Am J Cardiol*. 2000;86:585–586.
8. Rasmussen K, Møller J. Total homocysteine measurement in clinical practice. *Ann Clin Biochem*. 2000;37:627–648.
9. Brott T, Adams HP Jr, Olinger CP, et. al. Measurements of acute cerebral infarction: a clinical)examination scale. Stroke. 1989 Jul;20(7):864-70
10. Falck Suzanne, Anthony Kiara . health line, High Homocysteine Level (Hyperhomocysteinemia).on January 2, 2018 (https://www.healthline.com/health/homocysteine-levels)
11. Del Ser T, Barba R, Herranz AS, Seijas V, López-Manglano C, Domingo J, Pondal M. Hyperhomocyst(e)inemia is a risk factor of secondary vascular events in stroke patients. *Cerebrovasc Dis*. 2001;12:91–98.
12. Brattström L, Lindgren A, Israelsson B, Malinow MR, Norrving B, Upson B, Hamfelt A. Hyperhomocysteinaemia in stroke: prevalence, cause, and relationships to type of stroke and stroke risk factors. *Eur J Clin Invest*. 1992;22:214–221
13. Lindgren A, Brattström L, Norrving B, Hultberg B, Andersson A, Johansson BB. Plasma homocysteine in the acute and convalescent phases after stroke. *Stroke*. 1995;26:795–800.
14. Eikelboom JW, Hankey GJ, Anand SS, Lofthouse E, Staples N, Baker RI.Association between high homocyst(e)ine and ischemic stroke due to large- and small-artery disease but not other etiologic subtypes of ischemic stroke. *Stroke*. 2000;31:1069–1075.
15. Tan NC, Venketasubramanian N, Saw SM, Tjia HT. Hyperhomocyst(e)inemia and risk of ischemic stroke among young Asian adults. *Stroke*. 2002;33:1956–1962.
16. McCully KS. Homocysteine and vascular disease. *Nat Med*. 1996;2: 386–389.
17. Bots ML, Lauber LJ, Lindemans J, Hofman A, Grobbee DE. Homocysteine, atherosclerosis and prevalent cardiovascular disease in the elderly: the Rotterdam study. *J Intern Med*. 1997;242:339–347.
18. Malinow MR, Nieto FJ, Szklo M, Chambless LE, Bond G. Carotid artery intimal-medial wall thickening and plasma homocyst(e)ine in

asymptomatic adults. *Circulation*. 1993;87:1107–1113.

19. Streifler JY, Rosenberg N, Chetrit A, Eskaraev R, Sela BA, Dardik R, Zivelin A, Ravid B, Davidson J, Siligsohn U, Inbal A. Cerebrovascular events in patients with significant stenosis of the carotid artery are associated with hyperhomocysteinemia and platelet antigen-1 (Leu33Pro) polymorphism. *Stroke*. 2001;32:2753–2758.
20. Gheyath AlGawwam,Asaad Adil Mnaather,Akram Al-Mahdawi et al. Serum aspartic acid as a Marker of epilepsy.*Global journal of health science.*2019;11:142-143.