Hyperhomocysteinemia - An unidentified risk factor for stroke in our population

Sabaa Asif  
Ziauddin Medical University Hospital

Bashir A Soomro  
Ziauddin Medical University Hospital

Kanwal Sartaj  
Ziauddin Medical University Hospital

Shafaq Alvi  
Ziauddin Medical University Hospital

Follow this and additional works at: http://ecommons.aku.edu/pjns

Part of the Neurology Commons

Recommended Citation
Asif, Sabaa; Soomro, Bashir A; Sartaj, Kanwal; and Alvi, Shafaq (2015) "Hyperhomocysteinemia - An unidentified risk factor for stroke in our population," Pakistan Journal of Neurological Sciences (PJNS): Vol. 10 : Iss. 2 , Article 2.  
Available at: http://ecommons.aku.edu/pjns/vol10/iss2/2
HYPERHOMOCYSTEINEMIA- AN UNIDENTIFIED RISK FACTOR FOR STROKE IN OUR POPULATION

Sabaa Asif*, Bashir A.Soomro, Kanwal Sartaj*, Shafaq Alvi

*Resident, Department of Medicine, Ziauddin Medical University Hospital.

Correspondence to: Bashir A.Soomro, 43/II Zulfiqar Street No: 03, PhaseVIII DHA, Karachi, Postal Code: 75500, Email: Basoomro@gmail.com

Date of Submission: 29 August 2014, Date of Revision: 7 January 2015, Date of Acceptance: 6 February 2015

ABSTRACT

Introduction: Various studies show that moderate elevation of plasma homocysteine level has been associated with increased risk for cardiovascular and cerebrovascular disease. Objective: To observe the frequency of increased homocysteine level in ischemic stroke patients; and its association with other risk factors. Methodology: Observational pilot study was conducted on a sample of 75 ischemic stroke patients, enrolled regardless of their age, gender and comorbidities, at Ziauddin university hospital, Karachi. Fasting serum homocysteine, folate and vitamin B12 levels were measured. Results were interpreted using spss 20.0. Results and Discussion: Mean homocysteine level in our population was 19.51 (SD: 11.47) micromol/l. It was higher in groups with vitamin B12 and folic acid deficiency, difference being statistically significant (p=0.013 and 0.017, respectively). Males had greater propensity to hyperhomocysteinemia; the mean homocysteine value being higher, and the difference, statistically significant (p=0.010). Other factors that affect homocysteine levels were also evaluated, that is hypertension, increased cholesterol levels and smoking. There was no significant statistical difference in the homocysteine value between the groups of patients who had these risk factors and the groups that did not (p=0.747, 0.252 and 0.565, respectively). Conclusion: It was speculated that hyperhomocysteinemia is an imperative risk factor for stroke.

INTRODUCTION

Homocysteine has gained significant attention in the last decade for its atheroogenic properties. Various studies have shown that moderate elevation of the plasma level of this metabolite has been associated with increased risk for cardiovascular and cerebrovascular disease (1,2,3). Besides causing atherosclerosis, raised homocysteine levels also increase the risk of vascular dementia and Alzheimer’s disease (3). Homocysteine levels may be moderately elevated secondary to deficiency of enzyme co-factors involved in homocysteine metabolism (i.e. Vitamin B12, B6 and folate) and genetic polymorphism in methylenetetrahydrofolatereductase (enzyme involved in homocysteine metabolism) (3,4). In addition, plasma levels of homocysteine are influenced by other factors. Increased levels are associated with high blood pressure, elevated cholesterol levels, smoking, increasing age and gender (more prevalent in males) (3,6). Vascular injury induced by moderately elevated levels of homocysteine is characterised by intimal thickening, disruption of elastic lamina, smooth muscle proliferation, platelet accumulation, and formation of platelet plugs (7,8). Studies are now being done to determine whether vitamin therapy reduces the risk of ischemic stroke and stroke-related disability (9). HOPE-2 (Heart Outcomes Prevention Evaluator 2) study shows that although homocysteine-lowering therapies did not improve the outcome of cardiovascular death, MI and stroke, but the risk of stroke was reduced by around 25%, after a fair duration of treatment of three years in persons younger than 70 years with untreated hyperlipidemia, not receiving antiplatelets and with hyperhomocysteinemia or folate and vitamin B12 deficiency (10,11). Although the VISP (Vitamin Intervention for Stroke Prevention) trial showed that high-dose multivitamin therapy did not help in preventing recurrent stroke, the control agent used in the trial contained small doses of vitamin B6, B12, and folic acid, and the reduction of homocysteine level was less than that expected in the study. 12 Besides these, four meta-analyses reporting on the benefit of folic acid or vitamin B supplementation have been published in 2010 (13,14,15,16).

OBJECTIVE

To observe the frequency of increased homocysteine levels in patients with ischemic stroke, presenting to our private tertiary care centre, regardless of their age, gender, race and social status; and its association with other risk factors.
RESULTS

Out of the 75 enrolled patients, 33(44%) had moderately elevated homocysteine level, 10(13.3%) had severely elevated level of more than 30 μmol/l (Table 1). The mean homocysteine level was 19.52 (SD: +/- 11.47) μmol/l, with the minimum being 7.02 μmol/l and the maximum 50 μmol/l. The mean folate level was 7.15 (SD: +/- 4.51) ng/ml, with a minimum of 1.12 ng/ml and a maximum of 21.50 ng/ml. The mean vitamin B12 level was 432.55 (SD: +/- 293.53) pg/ml; minimum, 150 pg/ml and maximum, 1000 pg/ml.

Table 2

<table>
<thead>
<tr>
<th>Homocysteine Level (μmol/l)</th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal &lt;14</td>
<td>32</td>
<td>42.7</td>
<td>42.7</td>
<td>42.7</td>
</tr>
<tr>
<td>Moderately Elevated &gt;14</td>
<td>33</td>
<td>44.0</td>
<td>44.0</td>
<td>86.7</td>
</tr>
<tr>
<td>Severely Elevated &gt;30</td>
<td>10</td>
<td>13.3</td>
<td>13.3</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>75</td>
<td>100.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION

The study showed a strong association between hyperhomocysteinemia and stroke, with 44% of the patients having moderately elevated levels and 13.3% having severely elevated levels of more than 30 μmol/l, making a total of 53.3% of patients. Various studies have shown that homocysteine levels increase with age (3,6), although our study speculates that there is no association between hyperhomocysteinemia and increasing age, as the difference in mean homocysteine levels was statistically not significant. We also looked for association between increased homocysteine levels and gender. As described in different studies previously (3,6), our study also showed a significant difference in mean homocysteine levels between males and females. Males had higher propensity to hyperhomocysteinemia than females. Deficiency of enzyme co-factors involved in homocysteine metabolism (i.e. Vitamin B12, B6 and folate) and genetic polymorphism in methylenetetrahydrofolate reductase (enzyme involved in homocysteine metabolism) are alleged to cause hyperhomocysteinemia (3,4). In our patients, the patients who were deficient in vitamin B12 and folic acid had a greater predilection to hyperhomocysteinemia than those having normal vitamin B12 and folic acid values, with a significant statistical difference in the mean homocysteine value between the two groups. Similarly, other variables that are individually associated with both hyperhomocysteinemia and ischemic stroke, were evaluated, that is hypertension, increased cholesterol...
levels (5) and smoking (3,6). The group of patients that were non-hypertensive also had an elevated mean homocysteine value and the difference in the mean level between the hypertensive and non-hypertensive group was statistically not significant. In the same way, there was no significant statistical difference in the mean homocysteine value between the group of patients having increased cholesterol levels and that with normal cholesterol levels. So, it can be speculated that increased cholesterol levels do not directly relate to hyperhomocysteinemia. Non-smokers had a higher mean homocysteine value, compared to the smokers, the difference being statistically non-significant, showing that there is no association between this variable and hyperhomocysteinemia.

CONCLUSION

It is speculated that hyperhomocysteinemia is an imperative risk factor for stroke in our population. Although the patients had other risk factors as well that individually contribute to stroke but the role of homocysteine in vascular diseases should be considered. Large studies should be conducted on our local population, to determine the absolute risk of having high levels of homocysteine on stroke, and trials should be conducted to observe the effect of homocysteine-lowering therapy on its incidence. Many studies have shown that the routine use of such therapies does not decrease the risk of stroke, but there is evidence that homocysteine-lowering therapy helps in secondary prevention in individuals with ischemic stroke. Since homocysteine-lowering therapy does not appear to have any major side effects and is rather cost-effective, it should be considered for use in these patients (though with caution in patients with renal failure or decreased glomerular filtration rate, in whom more active forms i.e. methylcobalamin and tetrahydrofolate are recommended).17

REFERENCES


5. Nygard O, Vollset SE, Refsum H, Stensvold I,


Conflict of Interest: Author declares no conflict of interest.

Funding Disclosure: Nil

Author’s contribution:

Dr.Saba Asif: Study concept and design, protocol writing, data collection, data analysis, manuscript writing, manuscript review

Dr. Bashir Soomro: Study concept and design, protocol writing, data collection, data analysis, manuscript writing, manuscript review

Dr. Kanwal Sartaj: Data collection, data analysis, manuscript writing, manuscript review

Dr.Shafaq Alvi: Data collection, data analysis, manuscript writing, manuscript review