DOI: 10.14260/jemds/2014/4093

ORIGINAL ARTICLE

OCULAR MORBITIES ASSOCIATED WITH HYPERHOMOCYSTENEMIA

H. N. Sowbhagya[1], Kiran Kumar L[2], Minal Kothari[3], Nivedhitha Nikhil[4], Deepthi U. S[5]

HOW TO CITE THIS ARTICLE:
H. N. Sowbhagya, Kiran Kumar L, Minal Kothari, Nivedhitha Nikhil, Deepthi U. S. "Ocular Morbities associated with Hyperhomocystenemia". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 74, December 29; Page: 15507-15510, DOI: 10.14260/jemds/2014/4093

ABSTRACT: STUDY DESIGN: Retrospctive study**. MATERIAL AND METHODS:** 49 patients of hHyc referred from various departments for ophthalmic opinion are included in the study. All cases were evaluated for anterior segment and posterior segment presentations. Field test was done for cases who had optic nerve involvement and cerebral infarcts. **RESULTS:** out 49 cases 25 cases had significant ocular findings mainly vascular involvements and sequlaes, like Retinal branch vein occlusion(BRVO), papillodema, visual field defects, Non arteritic anterior ischemic optic neuropathy (NA-AION) and optic disc pallor and 49%(24 patients) had no ocular findings. All cases were of moderate to intermediate hHyc and could undergo all the tests. One case with severe brain ischemia evaluated in medical casualty died. **CONCLUSION:** hHyc can present with varied vascular and ischemic ocular findings. Study shows the need for hHyc evaluations in all cases ocular ischemic and vascular catastrophes.

KEYWORDS: Hyperhomocystenemia, Retinal branch vein occlusion, Non arteritic anterior ischemic optic neuropathy, field defects, cerebral ischemia.

MESHTERMS: Hyperhomocystenemia, branch retinal vein occlusion, retinal ischemia, Non arteritic anterior ischemic optic neuropathy, brain infarct, optic disc pallor, optic disc edema, cerebral venous thrombosis.

INTRODUCTION: Homocysteine is a sulphur containing amino acid. It is an intermediate in the synthesis of methionine, and methyl group donor, S adenosyl methionine. It is metabolised by one of the 2 pathways remethylation or transsulfuration. Abnormalities of these lead to Hyperhomo-cysteinemia (hHcy). There are various causes of hHcy but mainly it is due to enzyme deficiencies – cystathionine β synthase, methionine synthase, 5-methyltetrahydrofolate reductase or vitamin deficiencies-folate, vitamin B6 or B12.[1] hHcy is observed in approximately 5% of the general population and is associated with an increased risk of many disorders, including vascular and neurodegenerative diseases, autoimmune disorders, birth defects, diabetes, renal diseases, osteoporosis, neuropsychiatric disorders and cancer.[1] The thrombo embolic effect of a high total plasma homocysteine level has been documented as early as 1968[2]. In the ocular system many lines of evidence indicate that hHcy is a risk factor in a variety of disease including retinal atherosclerosis, cataract, glaucoma, exudative age related macular degeneration, macular and optic atrophy due to retinal vascular occlusions and non arteritic ischemic optic neuropathy.[3]

In this study we have observed the various ocular manifestations of patients with hHcy. Since retina is the window for visualization of the body's circulation and possible to see the findings.

MATERIALS AND METHODS: This study was conducted between June 2012 and September 2014 in Kempegowda Institute of Medical Sciences and Research Centre, Bangalore India. All patients who were referred for ophthalmological opinion from the medicine, neurology and cardiology department

DOI: 10.14260/jemds/2014/4093

with hHcy were evaluated. Hyperhomocysteinemia was defined as having a serum level greater than 15μmol/L. It was further categorized as moderate, intermediate, and severe if the level was 16–30, 31–100, and more than 100μmol/L, respectively. Serum Homocysteine levels was estimated using enzymatic recycling method. Total number of hHcy subjects screened were 49. Visual acuity was tested by Snellens chart. The best corrected visual acuity was recorded. If the person could not correctly recognize the top letter of the chart, visual acuity was noted using the finger counting method. Anterior segment evaluation done using slit lamp and refraction was done by using Huwitz autorefractometer.

Intra ocular pressure was recorded using Perkins tonometer. Posterior segment evaluation was done after dilating with tropicamide- phenylephrine eye drops using indirect ophthalmoscope (Keeler), 90D panfundoscopy lens and goldmann 3 mirror examinations. Visual field analysis (where possible) was done using Humphrey visual field analyser. In selected cases, we performed fluorescein angiography. Other investigations like radiological investigations such as CT, MRI, MR venogram, and lumbar puncture were reviewed from the records. Haematological workup such as lipid profile, hemogram, biochemistry and serology were reviewed.

RESULTS: 49 patients with Hyperhomocysteinemia underwent ophthalmological evaluation. Out of this 33(67%) were male patients and 16(33%) were females. The mean age group of presentation was 34.8yrs (ranging from 20yrs - 60yrs). 30 patients (61%) had moderate hHcy, 18patients (37%) had intermediate hHcy and 1(2%) had severe hHcy.55% of the patients had additional co morbid conditions like diabetes and hypertension and 45% had no co morbid conditions. 44.8% (22patients) presented with headache, giddiness etc, 38.7% (19 patients) presented with various visual disturbances like detective vision, field loss and 16.3 % (8 patients) had no-ocular symptoms. 51%(25 patients) showed ocular findings such as BRVO, papillodema, visual field defects, NA-AION and optic disc pallor and 49% (24 patients) had no ocular findings.

Sl no	Manifestation	No's	%	Comments	Visual fields
1.	Papillodema	6	12.2%	2cases were due to cerebral venous thrombosis on MR venogram. 1 case of Benign intracranial hypertension. 3 were idiopathic.	4 patients had normal fields and 2 had peripheral constriction
2.	Branch retinal vein occlusion.	10	20.4%	Most common involved vessels were STVO followed by ITVO	
3.	Non Arteritic anterior ischemic optic neuropathy (NA-AION)	2	4.1%		1 patient showed arcuate field defects, 1had inferior altitudinal defect
4	Temporal Optic disc pallor	4	8.2%	Brain infarcts most common vessel involved was MCA and PCA	3 patients showed homonymous hemianopic field defects
5	Normal fundus with field defects.	3	6.1%	Brain ischemia	2 showed homonymous hemianopic field defects,

2 patients with papillodema showed cerebral venous sinus thrombosis, 1 had benign intracranial hypertension features and rest 3 showed normal MRI. 7 patients showed infarctions in

the brain. Most common vessel involved was the Middle cerebral artery followed by the posterior cerebral artery. Out of 10 vein occlusions 7 had superotemporal vein occlusion and 3 had inferotemporal vein occlusion.

DISCUSSION: At the cellular level hHcy causes vascular endothelial damage, proliferation of the vascular smooth muscle cells, elevated lipid peroxidation leading to free radical formation. By these pathophysiological processes hHcy can produce vascular occlusion and neovascularisation. Hyperhomocysteinemia is reported as an independent risk factor for systemic and ocular vasoocclusive disorders, including nonarteritic ischemic optic neuropathy (NAION), central retinal artery occlusion (CRAO), and central retinal vein occlusion (CRVO), especially in young patients[4, .5].It has been reported that as many as 17% of young patients with NAION may have isolated hyperhomocysteinemia as the risk factor.[6]

In our study 4.1% of patients with hHcy presented with NAAION. In a study conducted in Indian subcontinent[6] Hyperhomocysteinemia was a significant independent risk factor for RVO. However severity of hHcy levels and types of RVO had no "dose response" relationship. In our study branch retinal vein occlusion (BRVO) was the most common ocular manifestation (20.4%) of hHcy. In a study done Gore A D et.al in 66% of the eyes with BRVO, superior temporal retinal vein was the most common vessel involved followed by 22-43% of eyes with occlusion of major branch in inferior temporal quadrant. Increased plasma homocysteine is associated with both retinal vein and retinal artery occlusion and the elevation being greater in vein occlusion.[7]

In a case series presented by Virendra Sachdeva et al,[8] from LVPEI, India 4 cases of isolated abducent nerve palsy was associated with hHcy. However we did not come across any such cases.

In our study we came across 6 patients with papillodema and hHcy, 4 of which had a normal MRI and the other 2 had cerebral venous sinus thrombosis diagnosed on MR venogram. A study done by Ida Martinelli et al[9] shows that hyperhomocysteinemia increases the risk of cerebral vein thrombosis by approximately 4-fold.In our study 14.3 % of hHcy had silent ischemia of the brain with ocular presentations like optic dic pallor in 4 cases, field defects in 5cases. elevated levels of total homocysteine (tHcy) an amino acid are an independent risk factor for silent stroke, even in healthy middle-aged adults.[10,11,12.]

REFERENCES:

1. Brustolin S, Giugliani R, Felix TM. Genetics of homocysteine metabolism and associated disorders. Brazilian Journal of Medical and Biological Research Online Provisional Version. December 4, 2009.
2. Ratnoff OD. Activation of Hageman factor by L-homocystine. Science 1968; 162: 1007-9. [PUBMED].
3. N. Manresa, J. Mulero and P. Zafrilla Homocysteine: Biosynthesis and Health Implications Hyperhomocysteinemia and Association of Eye Disease (pp. 165-190).Nova science publishers https://www.novapublishers.com /catalog / product_info.php?products_id=48123.
4. Pianka P, Almog Y, Man O, Goldstein M, Sela BA, Loewenstein A. Hyperhomocysteinemia in patients with nonarteritic anterior ischemic optic neuropathy, central retinal artery occlusion, and central retinal vein occlusion. Ophthalmology 2000; 107: 1588-92.

DOI: 10.14260/jemds/2014/4093

5. Ravi C, Ramesha K, Sachdeva V, Pathengay A, Rao BV. A case of presumed association of Hyperhomocysteinemia-with NAION and Cilioretinal artery obstruction. Asian J Ophthalmol 2009; 11: 32-4.
6. Kawasaki A, Purvin VA, Burgett RA. Hyperhomocysteinemia in young patients with non-arteritic anterior ischaemic optic neuropathy. Br J Ophthalmol 1999; 83: 1287-90.
7. Gore AD, Rao GS, Gore MA, Desai AR. Multiple extra macular branch retinal vein occlusions in hyperhomocysteinemia. Indian J Ophthalmol 2014; 62: 489-91.
8. Sachdeva V, Mittal V, Pathengay A, Kekunnaya R, Gupta A, Rao BV. Isolated abducens nerve palsy with hyperhomocysteinemia: Association and outcomes. Indian J Ophthalmol 2013; 61: 598-600.
9. Ida Martinelli, Tullia Battaglioli, Paola Pedotti, Marco Cattaneo, andPier M. Mannucci. Hyperhomocysteinemia in cerebral vein thrombosis;August 15, 2003; Blood: 102 (4)
10. Vermeer, SE; Van Dijk, EJ; Koudstaal, PJ; Oudkerk, M; Hofman, A; Clarke, R; Breteler, MM (2002). "Homocysteine, silent brain infarcts, and white matter lesions: The Rotterdam Scan Study". Annals of neurology 51 (3): 285–9. doi:10.1002/ana.10111. PMID 11891822.
11. Seshadri, S; Wolf, PA; Beiser, AS; Selhub, J; Au, R; Jacques, PF; Yoshita, M; Rosenberg, IH et al. (2008). "Association of plasma total homocysteine levels with subclinical brain injury: Cerebral volumes, white matter hyperintensity, and silent brain infarcts at volumetric magnetic resonance imaging in the Framingham Offspring Study". Archives of neurology 65 (5): 642–9. doi:10.1001/archneur.65.5.642. PMC 2700952. PMID 18474741.
12. Matsui, T; Arai, H; Yuzuriha, T; Yao, H; Miura, M; Hashimoto, S; Higuchi, S; Matsushita, S et al. (2001). "Elevated plasma homocysteine levels and risk of silent brain infarction in elderly people". Stroke; a journal of cerebral circulation 32 (5): 1116–9. doi:10.1161/01.STR.32.5.1116. PMID 11340219.

AUTHORS:

1. H. N. Sowbhagya
2. Kiran Kumar L.
3. Minal Kothari
4. Nivedhitha Nikhil
5. Deepthi U. S.

PARTICULARS OF CONTRIBUTORS:

1. Professor and HOD, Department of Ophthalmology, RGUHS.
2. Assistant Professor, Department of Ophthalmology, RGUHS.
3. Junior Resident, Department of Ophthalmology, RGUHS.
4. Junior Resident, Department of Ophthalmology, RGUHS.
5. Junior Resident, Department of Ophthalmology, RGUHS.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. H. N. Sowbhagya,
No.41-42/45,
Sreegurukrupa, 7th Cross,
Saraswathipuram, Nandini Layout,
Bangalore-560096.
E-mail: drhnsowbhagyaappaji@gmail.com

Date of Submission: 01/12/2014.
Date of Peer Review: 02/12/2014.
Date of Acceptance: 19/12/2014.
Date of Publishing: 26/12/2014.