A STUDY ON THE TYPE AND MORPHOLOGY OF ATHEROMATOUS PLAQUES IN ISCHEMIC STROKE IN A GOVERNMENT HOSPITAL IN WEST BENGAL

Physiology

Dr. Debalina Sengupta	Assistant Professor, Department of Physiology, Nil Ratan Sircar Medical College, Kolkata-700014
Dr. Md. Sadique Mallick*	Associate Professor, Department of Physiology, Nil Ratan Sircar Medical College, Kolkata-700014 *Corresponding Author

ABSTRACT

INTRODUCTION: Cerebrovascular accident or stroke is one of the commonest neurological disorder affecting mainly the elderly population worldwide. Atherosclerosis is a major cause of stroke both ischemic and haemorrhagic.

METHODS: This observational study was done with the aim of finding the type of atheromatous plaque and their incidence, unilateral or bilateral in ischemic stroke patients. After Ethical clearance 50 elderly patients (age group 50-70) admitted in a government hospital in Kolkata, West Bengal were taken.

RESULTS: After proper clinical examination, blood lipid profile, ultrasonographic evaluation of Carotid Intima Media Thickness it was found that pure single sided plaques (80.56%) were more common in cerebral ischemia and soft plaques(66.67%) were more common than calcified plaques.

CONCLUSION: Single sided and soft plaques in cerebral ischemia were more common than calcified plaques.:

KEYWORDS

Ischemic Stroke, Atheromatous Plaque, Carotid Intima Media Thickness

INTRODUCTION:

Cerebrovascular accident or stroke is a major cause of morbidity and mortality worldwide. This may result from brain infarction or hemorrhage. Majority (80%) are due to ischemic cerebral damage as a result of decrease in cerebral perfusion pressure[1].Atherosclerosis is a progressive disease characterized by accumulation of lipids and fibrous elements in the large arteries[2].The early lesions of atherosclerosis consists of sub endothelial cholesterol engorged macrophages called foam cells. More advanced lesions are characterized by the accumulation of lipid rich necrotic debris and smooth muscle cells. As the atheromatous plaque progresses, it may exhibit calcifications, ulcerations at the luminal surface and hemorrhage due to growth of blood vessels from the media of vessel wall[3,4]. The main mechanism of stroke related to pathology of the carotid artery is thought to be embolism from a fissured or ruptured plaque. Unstable plaques have thin fibrous cap, high lipid content like triglycerides are vulnerable to rupture leading to thromboembolism. An estimated 80% of strokes are thromboembolic in origin, often with carotid plaque as the embolic source[3]. Carotid Doppler studies on plaque morphology show that anechogenic (weakly reflecting ultrasound) or heterogeneous plaques carry a higher risk of subsequent neurological symptoms in comparison with homogenous or echogenic plaques that strongly reflect ultrasound[5,6,7,8].Thus this study is intended to associate the incidence of carotid plaque in relation to cerebral ischemia through Carotid Doppler Study.

MATERIALS AND METHODS

An observational, case control type of study[9] was conducted in the Department of Physiology in collaboration with Department. of Medicine, Radiology and Biochemistry at R.G.Kar Medical College, Kolkata- 700004. After receiving approval from the Ethics committee for human experiments of the institute selection of cases and controls were done by simple random sampling.

Study population included 50 stroke patients diagnosed by a neurologist as per WHO definition[10] and CT Scan (Computed Tomography) suggestive of cerebral infarction. Age sex matched 50 apparently healthy individuals were taken as "control group". All the volunteers were explained the purpose of the experiment, and a written consent was obtained from each of them.

Subject exclusion criteria :
- Severely ill subjects.
- Patients with cerebral hemorrhage.
- TIA without any CT Scan features of ischemic stroke.
- Intracranial neoplasm.
- Patients suffering from meningitis, neurocysticercosis or any infections.

- Head Injury.
- Intracranial aneurisms.
- AV malformations.
- Any cardiac source of embolism.
- H/O intake of any lipid lowering drugs.
- H/O Smoking.
- Coronary Heart disease

Subject inclusion criteria :
1. Diagnosed stroke patients as per WHO definition[10] as "Rapidly developing clinical signs of focal or global neurological deficits lasting for 24 hours or longer or resulting in death with no apparent cause other than vascular origin".
2. Patients admitted with cerebrovascular accident confirmed to be ischemic in nature on CT scan.
3. Subjects with first attack of stroke were chosen.

Age: The interest of this study is focused on elderly age group[11] and was aimed at 50-70 yrs age group of subjects. The controls were apparently healthy and age and sex matched with cases.

Study parameters History and Physical Examination with examination of the Nervous System in details. Biochemical Tests: (1) Lipid Profile (after 12 hrs overnight fasting) for Cholesterol (CHOD/PAP Method), Triglycerides by (GPO/PAP Method) LDL: HDL ratio. (HDL by PEG Precipitation method and LDL by Friedewald's formula (Total Cholesterol) (Triglycrides/5) (HDL Cholesterol). Carotid Doppler Study was performed only with appropriate high frequency transducers with patient in supine position. High resolution B mode, colour Doppler ultrasonography of both carotid arteries were performed with an ultrasound machine (Image Point HX)) equipped with a 10 MHz linear array transducer. The maximum IMT was measured at the near and far walls of the common carotid artery, the bifurcation, and the internal carotid arteries and was expressed as a mean aggregate value. In the study values greater than 0.8 mm (0.08 cm) were considered abnormal [12,13,14]. Atheromatous carotid plaque was evaluated by the Doppler study. Plaque texture is generally classified as being homogenous or heterogeneous [15,16].Homogenous plaque has a uniform echo pattern and a smooth surface. The uniform acoustic texture corresponds pathologically to dense fibrous connective tissue. Calcified plaque produces posterior acoustic shadowing and is common in asymptomatic individuals. Heterogenous plaque has a more complex echo pattern. Heterogeneous plaque is characterized pathologically by containing intraplaque hemorrhage and/or deposits of lipid, cholesterol, and proteinaceous material[16]

Plan of statistical analysis

Data were compiled in MS excel worksheet (Office document 2007) and analysis done in SPSS VERSION 17 statistical software (for windows).

Results were statistically analyzed using following statistical tests :
Chi-square test.
Independent Sample "T-test".
Multiple Regression Analysis.

Mean and Standard deviation were calculated from the results of individual parameter. P value of <0.05 was considered to be significant and P<0.001 as highly significant. The results were calculated within 95% confidence limits.

RESULTS

Basic characteristics of subjects.

Basic characteristics of case (N=50)(Mean±SD) are , age (yrs) 61.72±6.93 systolic BP (mm of Hg) 154.60±16.13 ,diastolic BP (mm of Hg) 97.72±16.07 fasting Blood Sugar (mg/dl)117.92±33.85 >0.05 and post Prandial Blood Sugar (mg/dl) 134.24±60.62

TABLE 1: DISTRIBUTION OF PATIENT ACCORDING TO THE PLAQUE FORMATION.

Total Plaque	No plaque	p-value
72% (N=36)	28% (N= 14)	<0.0001

TABLE 2

SINGLE SIDED PLAQUE	PURE BOTH SIDED PLAQUE
• 80.56%	19.44%
• (n=29)	(n=07)
Chi- square	24.507
DF	1
Significance level	P<0.0001

Comments: There is a highly significant difference between the patients having pure single and both sided plaques (p<0.0001).

TABLE3:

Pure Rt. Sided Plaque: 16/36, Pure Lt. Sided Plaque: 13/36

Pure Rt sided Plaque	Pure Lt Sided Plaque
44.45% (n=16)	36.12% (n=13)
Chi-Square	0.231
DF	1
Significance level	P= 0.6310

TABLE 4: Total Soft Plaque: 24/36   Total Calcified Plaque: 12/36

Total Soft Plaque	Total Calcified Plaque
66.67% (n=24)	33.34% (n=12)
Chi-square	6.725
DF	1
Significance level	P=0.0095

Comments: There is a significant difference (p=0.0095) between the patients having total soft and total calcified plaques.

DISCUSSION

It is seen that pure single sided plaques are more common in cerebral ischemia than pure both sided plaques as there is a highly significant difference between the patients having pure single and both sided plaques (p<0.0001). It is also seen that soft plaques are more common in cerebral ischemia than calcified plaques as there is a significant difference between the patients having soft and calcified plaques (p=0.0095).This study also shows that there are more soft plaques in the cases and that they are more on the right side, although this distribution is not significant (p>0.05).

Kitamura A et al[17] reported that wall thickening of the CCA and the formation of uncalcified plaque in the ICA were positively associated with an increased risk of stroke in elderly Japanese men. In a population-based cohort, it was found that carotid plaque with irregular surface increased the risk of ischemic stroke(IS) 3-fold. The cumulative 5-year IS risk among individuals with an irregular plaque surface was over 8%, whereas those with regular plaque had <3% 5-year risk. These data suggest that plaque surface irregularity, even after adjusting for degree of stenosis and plaque thickness, is an independent predictor of IS[18]. Held C et al[19]and Hunt et al[20]found in their studies that presence of regular plaque surface or plaque alone

increased the risks of vascular outcomes, although these associations did not reach statistical significance. Hollander M et al[21] showed that although the Rotterdam Study reported an increased IS risk among those with 5 to 6 plaques, presence of >1 carotid plaque in their study was not significantly associated with IS but increased the risk of MI. Lovett JK et al[22] in his study said that the exact mechanisms linking irregular plaque surface and ischemic stroke are unclear. *BusinaroR et al*[23] Elkind MS et al[24] *LombardoAet al*[25], Lovett JK et al[26] observed that proinflammatory markers are elevated in patients with complex or unstable carotid plaques, implying an inflammatory mechanism in plaque vulnerability and ipsilateral stroke. Our study also agrees to some aspects of the previous studies. In this study it is seen that unstable or soft plaques are more responsible for causing cerebral ischemia and stroke.

CONCLUSION

From the above study it can be concluded that altered lipid profile is associated with cerebral ischemia by increasing carotid intima media thickness (IMT). Gradual deposition of lipoproteins in the carotid arteries leads to increased carotid artery Intima Media Thickness (IMT) and gradually plaque formation occurs. In our study soft plaques are more common in cerebral ischemia than calcified plaques . Rupture and dislodgement of a soft plaque leads to embolism and subsequent ischemic stroke.

Limitations of the study

- Sample size is small.
- Study period was only one year.
- Follow up was not possible.
- Detailed echomorphology of the plaque was not studied.

REFERENCES

1. Uma N, Chugh SK , Harshwardhan, Geol A, Gopal D. (1999).Echocardiography   in patients with cerebral infarction. JAPI 47, 291 – 293.
2. LuissAJ,Atherosclerosis (2000).Nature;407:233-41
3. Bassiouny HS et al.(1997). Juxtaluminal location of plaque necrosis and neoformation in symptomatic carotid stenosis. JVascSurg, 26,585-94.
4. Kiechl S,Willeit J.(1999).The natural course of atherosclerosis. Part II:vascular remodeling.Bruneck Study Group..Arterioscler Thromb Vasc Biol,19,1491-8.
5. Barnett HJM, Taylor DW ,Eliaszw M.(1998). For the North American Symptomatic Carotid End arterectomy trial   Collaborators. N Eng J Med,339 ,1415-2.
6. MRC European Carotid Surgery Trial(1991): interim results for symptomatic patients with severe (70-99%) or with mild (0-29%) carotid stenosis. European Carotid Surgery Trialists' Collaborative Group. Lancet,. 337(8752), p. 1235-43.
7. Neurology in Clinical practice: Principles of Diagnosis & Management-4thEd.Volume 1;Walter G.Bradley,Robert B.Daroff,Gerald M..Fenichel, Joseph Jankovie-Neuroepidemiology; Mitchell T.Wallin & John F.Kurtzke--(Pg 777-780)
8. Executive Committee of the Asymptomatic Carotid Atherosclerosis   study. (1995). JAMA,273:1421-8.
9. Park K (2009) Textbook of Preventive and Social Medicine.Ptinciples of Epidemiology and Epidemiologic Methods, Analytical Epidemiology; Ed 3:p 67.
10. Bamford J, Sandercock P, Dennis M, Burn J, Warlow C. (1991) Classification and natural history of clinically identifiable subtypes of cerebral   infarction. Lancet.,337,1521–1526.
11. Bhattacharya S, Prasarsaha S, Basu A, Das K. (2005) A 5 year prospective study of incidence, morbidity and mortality stroke profile on stroke in a rural community of Eastern India. J Indian Med Assoc, 103 (12), 655-9
12. Bell FP, Adamson I, Schwartz CJ: Aortic endothelial permeability to albumin. (1974). Focal and regional patterns of uptake and transmural distribution of 1251- albumin in the young pig. ExpMol Puthol; 20, 51
13. Bell FP, Day AJ, Gent M, Schwartz CJ: (1975). Differing patterns of cholesterol accumulation and 3H-cholesterol influx in areas of the cholesterol-fed pig aorta identified by Evans Blue dye. Exp Mol Pathol ,22,366 .
14. Brandley WG. Ischemic cerebrovascular disease.In: Brandley WG, Daroff RB, Fenichel GH, Joseph J, editors.   Neurology in clinical practice. 4th edn. USA: Butterworth Heinemann
15. Bluth EI, Stravros AT,Marich KW, et al.(1988l). Carotid duplex sonography: A multicenter recommendation for standardized imaging and Doppler criteria.Radiographics,8,487-506.
16. Merritt CRB,Bluth EI. (1992)The future of carotid sonography.AJR; 158,37-39.
17. Kitamura A, Iso H, Imano H, Ohira T, Okada T, Sato S, Kiyama M, Tanigawa T, Yamagishi K, Shimamoto T. (2004). Carotid intima-media thickness and plaque characteristics as a risk factor for stroke in Japanese elderly men. Stroke., 35, 2788–2794.
18. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). (2001) JAMA, 285, 2486–2497.
19. Held C, Hjemdahl P, Eriksson SV, Bjorkander I, Forslund L, Rehnqvist N. (2001). Prognostic implications of intima-media thickness and plaques in the carotid and femoral arteries in patients with stable angina pectoris. Eur Heart J, 22, 62–72.
20. Hunt KJ, Evans GW, Folsom AR, Sharrett AR, Chambless LE, Tegeler CH, Heiss G. Acoustic shadowing on b-mode ultrasound of the carotid artery predicts ischemic stroke: the Atherosclerosis Risk In Communities (ARIC) study. Stroke. 2001; 32: 1120–112.
21. Hollander M, Bots ML, Del Sol AI, Koudstaal PJ, Witteman JC, Grobbee DE, Hofman A, Breteler MM. (2002) Carotid plaques increase the risk of stroke and subtypes of cerebral infarction in asymptomatic elderly: the Rotterdam study. Circulation ,105, 2872–2877.
22. Lovett JK, Gallagher PJ, Hands LJ, Walton J, Rothwell PM. (2004).Histological correlates of carotid plaque surface morphology on lumen contrast imaging. Circulation., 110, 2190–2197.
23. Hokanson,J.E. and Austin,M.A.(1996) Plasma triglycerides level is a risk factor for cardiovascular dis. Independent of HDL-cholesterol level:a meta-analysis of

population-based prospective studies. J. Cardiovasc. Risk, 3, 213-19.
24. Elkind MS, Cheng J, Boden-Albala B, Paik MC, Sacco RL. (2001) Elevated white blood cell count and carotid plaque thickness: the N orthern Manhattan Stroke Study. Stroke,32, 842–849.
25. Lombardo A, Biasucci LM, Lanza GA, Coli S, Silvestri P, Cianflone D, Liuzzo G, Burzotta F, Crea F, Maseri A. (2004) Inflammation as a possible link between coronary and carotid plaque instability. Circulation , 109, 3158–3163.
26. Lovett JK, Gallagher PJ, Hands LJ, Walton J, Rothwell PM. (2004)Histological correlates of carotid plaque surface morphology on lumen contrast imaging. Circulation,110, 2190–2197. END