Study Protocol

A Study Protocol on Assessment of ECG and Echocardiography Changes in Stroke Patients

Abstract:

Background: Ischemic stroke is accountable for about 80% of the first episode of cerebrovascular accidents. Cerebrovascular accident due to intracerebral hemorrhage is described as an abrupt onset of clinical signs of central nervous system dysfunction resulting from focal collection of blood inside the ventricular system or brain parenchyma, which is not caused by trauma. Stroke is reported as the most common cause of mortality in developed countries after cardiovascular problems. In cerebrovascular accidents, ECG changes like ST-T changes, QT prolongation, abnormal U waves etc have been reported. Also 2D echocardiographic changes have been reported in stroke patients. This study aims to assess different changes in electrocardiograph and 2D echo patterns cerebrovascular accident cases and their prognostic importance.

Objectives: To study variations in Electrocardiogram and 2D Echo in stroke patients in stroke patients and to rule out end organ insufficiency of vital organs.

Methodology: This will be a Prospective Cross-Sectional study. About 200 patients of Cerebrovascular accidents reporting to Dept of Emergency Medicine at AVBRH will be included in this study. All patients will undergo 12-lead electrocardiography, at the time of arrival to the hospital. CT scan/MRI will be performed within half an hour of reporting to Emergency Department. After management of stroke, 2D ECHO will be performed. Data of all patients will be analysed with appropriate statistical packages.

Expected outcome: A Significant correlation is expected between ECG changes and stroke.

Keywords: Electrocardiograph, Stroke, 2-D ECHO, Cardiovascular accidents

Introduction:

Definition of stroke, also called a cerebrovascular accident, is the fast onset of central nervous system defect that can be due to a vascular cause. Stroke Council of American Heart Association or American Stroke Association defined central nervous system infarction as spinal cord, brain or retinal cell death resulting due to ischemia depending on other pathological, radiological or other objective proof of spinal cord cerebral for retinal focal ischemic injury in a specific vascular distribution; or depending on clinical evidence of spinal cord, cerebral or retinal focal ischemic injury lasting more than 24 hours or until death and other etiologies excluded. Cerebrovascular accident is a fatal disorder. It is the most common cause of mortality after cardiovascular diseases and carcinoma in developed countries.(1)

Ischemic stroke is accountable for about 80% of the first episode of cerebrovascular accidents. Primary intracerebral hemorrhage was responsible for 10% cases and subarachnoid hemorrhage for 5%. A cerebrovascular accident due to intracerebral hemorrhage is described as an abrupt onset of clinical signs of central nervous system dysfunction resulting from focal collection of blood inside the ventricular system or brain parenchyma caused by trauma.

Above 20 years, cerebrovascular accidents occurrence in India was around 203 per 1 lakh population, attributing to about 1 million cases. Amongst all strokes, 12% of them are seen in the age group of less than 40 years of age(2). With age, there is increase in the risk of death due to stroke; among all deaths 2.4 % occur in old age (>70years of age).(3)

In various parts, the worldwide occurrence of stroke is 179 per 1,00,000 population overall prevalence ratio is 794 per 1 lakh population in western countries. Cerebrovascular accident or stroke is capable of inducing severe complication in both young and old people. They have major economic, psychological and social effects as well. Cerebrovascular injuries have created a great deal of interest in medical sector due to their high cost in economic terms and human injury. The physiological and anatomical mechanisms involved in brain heart interaction have been clarified in both animal and human research. Neurogenic mechanism was responsible for spreading the abnormal rhythm by stimulation of the sympathetic nervous system. The main site of vagal sympathetic and parasympathetic region involved in cardiac management has been identified as medulla oblongata. The hypothalamus in cardiac regulation is involved in both anatomical and physiological data (4). Electrical stimulation investigation revealed a post a really located cardiovascular sympathetic regulation and anteriorly situated parasympathetic control area(5). In reality, the central nervous system controls blood pressure, pulse rate, and motor tone and cardiac output and play an important role in myocardial metabolism and heart contraction. Catecholamine mediated cardiac changes are also triggered by an acute cerebrovascular accident (6).

In several diseases, ECG changes have been documented in cerebrovascular injuries. These changes are seen in T-wave, U-wave, ST-segment, QT interval and various arrhythmias. Myocardial infarction or myocardial ischemia may also mimic the changes in ECG.(7) Few studies have also demonstrated 2D echocardiographic changes in stroke patients in the form of Left Ventricular dysfunction , Aortic valve diseases, Mitral valve prolapse etc.(8) Many possible cardiac causes of embolism can be detected by 2D echocardiography, such as left atrial thrombus, patent foramen ovale, atrial septum aneurysm, valvular or myocardial disease, endocarditis or cardiac lesions and tumors like myxoma, etc. In addition, other cardiovascular dysfunctions may reveal possible clinical implications such as decreased left ventricular function, or any wall motion abnormality is that may warrant a modification in cardiology treatment.(9) Hence the present study is done to analyse different changes in 2 D echocardiography and ECG pattern in case of cerebrovascular accidents and determine the risk of end-organ insufficiency due to stroke in early detection and management.

Aim and Objectives:

AIM

- To study the changes of ECG and Echocardiography patterns in cases of cerebrovascular accident

- To assess whether these different changes have any prognostic significance in these cases

OBJECTIVES:

1. To study variations in ECG in stroke patients
2. To study variations or abnormalities in echo in stroke patients
3. To rule out end organ insufficiency of vital organs like Kidney and Heart.

Methods:

Study design: Prospective Cross-Sectional study.

Setting: The study will be conducted in the Acharya Vinoba Bhave Rural Hospital (AVBRH), a tertiary care hospital attached to Jawaharlal Nehru Medical College(JNMC) , situated in the rural area of Sawangi (Meghe) Wardha, in Central India.

DURATION OF STUDY

The duration of study will be from September 2020 to September 2022

Participants:

Cases:

Critically ill patients admitted in Emergency Medicine Department (IPD) AVBRH, Sawangi (Meghe) fulfilling the diagnostic or inclusion criteria.

INCLUSION CRITERIA:

Inclusion criteria: All patients with Acute Cerebrovascular Stroke

1. Age 20 - 80 yrs both sexes
2. Hypertensive
3. Diabetic
4. Peripheral vascular disease
5. Smokers

EXCLUSION CRITERIA:

1. Past History of stroke or >24 hrs of onset of symptoms
2. Traumatic
3. Diagnosed cases of Coronary artery disease
4. Patient not willing to participate in study

Study size: 150-200

Formula: n=4pq/l*l

p =71 ; q = 100 – p = 29

l = allowable error = 10% of p = 7.1

Hence n = 4*71*29/7.1*7.1

n~163 (so sample size should be upto 165)

Following admission a brief history regarding the clinical course of the stroke including risk factors like hypertension, diabetes mellitus, smoking, history of Ischaemic Heart Disease and rheumatic heart disease was taken. Brief cardiovascular examination and neurological examination were done in all the cases. The diagnosis of Cerebrovascular accidents will be made based on the following criteria:

- Temporal profile of clinical syndrome
- Clinical examination
- Computerised Tomography/Magnetic Resonance Imaging Brain

All patients will undergo-

1. 12 lead ECG
2. 2 Dimensional Echocardiography
3. Computerised Tomography/Magnetic Resonance Imaging Brain
4. Serum urea
5. Serum creatinine

ECG CRITERIA:-

- HR of less then 60/min will be labelled as bradycardia.
- HR of more then 100/min will be labelled as tachycardia.
- T- wave will be labelled unusual when T-wave inversion is seen in leads in 1,2, V3-V6 ideally, which should have been upwards. It may be different in 3, aVL,V1,V2.
- QTc prolongation: From the beginning of QRS complex to the end of T- wave, QT interval is measured. If we divide the actual QT by the square root of R-R interval (both measured in

seconds) the rate corrected QTc will be calculated. If QTc is more than 0.44m-sec it is labelled as QTc prolonged.

When exaggeration of U- wave voltage was noted, U wave was considered significant when appeared in more than 2-leads when appeared in leads in which it was not usually seen(other than V3-V4)

- Right Ventricular Hypertrophy : Dominant R-waves in right chest leads and R wave may be taller than S wave in leadV1, dominant S wave in V5 or V6
- Left Ventricular Hypertrophy - S wave depth in V1 + tallest R wave height in V5-V6 > 35 mm.

2D ECHO-

Parasternal, apical and sub-xiphoid windows were used in order to investigate the pathological changes of left atrium, left ventricle, aortic valve, mitral valve and their appendages

Statistical methods:

Statistical analysis will be done as per appropriate statistical tests and formulas.

Expected Outcomes/Results:

We expect changes in ECG which resemble myocardial ischemia and/ or lengthening of QT interval.

Discussion:

Many studies done earlier have shown that primary CNS dysfunction can also produce changes in ECG, hence abnormal changes in ECG in patients presenting with cerebrovascular accident poses diagnostic challenge. ECG changes can occur in patients presenting with cerebrovascular accidents even absence of any underlying cardiac disorders. Common ECG changes seen in stroke patients are QTc lengthening, ST-segment changes, T wave inversion, U waves, Sinus tachycardia but the value of these changes in predicting the mortality was poor. However, 2D echocardiography abnormality especially left ventricular dysfunction can predict mortality changes in patients with stroke should undergo ECG and 2D echocardiography as a part of initial assessment. WHO defined cerebrovascular disease as a central nervous system disorder with symptoms persisting more than 24 hours or leading to death before 24 hours. Symptoms are believed to be of nontraumatic origin after adequate investigation.(10)

In 76% of patients with SAH, **Khechinashivili G et al** (2002) registered irregularities in ECG of stroke patients such as ischemic like ECG changes aur QT prolongation , regardless of whether or not they had pre-existing heart disease, more than 90% of unassigned patients with ischemic cerebrovascular accident and intracerebral hemorrhage had such ECG changes. Still, the prevalence was much lower after exclusion of patient with pre-existing heart disease. (11)

Bozuluolcay M et al recorded that in patients with ECG abnormalities, the third day mortality rate was 14.8 percent, while in patients without ECG changes it was 8.5 %. In patients with ECG changes, the six month fatality rate was 38.9 % while in those with normal ECG death rate was 15.2%. (12)

Hanne Christensen et al found that patients suffering from atrial fibrillation, atrioventricular block, ST elevation and depression and inverted T waves have mortality at three months in multivariate research. Cause of vascular complications in patients can be attributable to changes in electrocardiogram.(13)

Jane G. Morris et. al. demonstrated that ECG defects occur in as many as 60 to 90 % of all cerebrovascular accident patients. QT prolongation and non-specific ST alterations are the most common changes recorded. The existence of underlying heart disease is most frequently indicated by these results. However even after removing patients with documented pre-existing cardiovascular disease that may be ECG defects in up to one-third of the patients. (14)

Of the 435 patients with Ischemic stroke, **Tiago Tribolet de Abreu, MD et al** found that 37.2% had findings suggesting blood thinners as beneficial in sinus rhythm: dilated cardiomyopathy was seen in 19.1% , previous anterior wall MI (6.2%), left ventricular systolic dysfunction with ejection fraction less than 35%(3.7%), stenosis of mitral valve with left atrial enlargement (1.6 %), intracardiac tumors (0.5%), valuar le prosthesis (0.2%) and >1 abnormality (5.5%). This research found that transthoracic echocardiography had treatment significance in 37.2 percent of ischemic stroke patients in sinus rhythm. In all sinus rhythm ischemic stroke patients, transthoracic echocardiography should be considered as an essential examination**.** (15)

Ramon et al suggested that 25% of ischemic cerebrovascular events accounted for cardioembolic cerebral ischemia. In addition, 23% of transient ischemic attack and 3.4 % of ischemic stroke accounted for transient ischemic attack of cardioembolic origin. Atrial fibrillation occurs in 99% of patients with atrial disrhythmia without structural heart defect. Mean age of these patients was 75 years, normal two-dimensional echocardiography results, 90% were without symptoms and 51% were already identified with atrial dysrhythmia and the outpatient environment, but there was no anticoagulation given (16).

In 81 patients common structural heart dysfunction with persistent sinus rhythm was diagnosed. In 73% of patients associated with intraventricular thrombosis and left ventricular systolic dysfunction was documented in 16%. In 99% of patients, structural heart defects were correlated with atrial fibrillation. in 52% of cases hypertensive left ventricular hypertrophy was reported followed by rheumatic mitral valve disease and left ventricular dysfunction. Mitral valve prolapse, atrial flutter, cardiac tumor, dilated cardiomyopathy , ischemic heart conditions, mitral annular calcification, and significant mitral regurgitation are other less common cardiac abnormalities in patients with structural cardiac disease. (16)

In a wide community of patients with cardioembolic ischemic incidents, **Ramon Pujadas Capmany et al** focused on the frequency of cardiological substrate and highlighted the possible causes of embolism. In cardioembolic stroke, the most common cardiac source of emboli is hypertrophic hypertensive cardiac disease exacerbated by atrial fibrillation, rheumatic mitral valve disorder, and systolic left ventricular dysfunction of ischemic non-ischemic cause. (16)

Nishede et al(17) - Severe cardiovascular disorders reported in patients with stroke were : Rheumatic heart disease in 37, congestive cardiomyopathy in 7, hypertensive cardiomyopathy in 19, calcification of mitral annulus in 29, prolapse of mitral valve in 9 and myocardial infarction in 10. In patients with ischemic cerebrovascular disease, rheumatic heart disease and mitral annular calcification were substantially more common than myocardial infarction and congestive cardiomyopathy for mitral valve prolapse.(17) Many articles from GBD study reflect the evidences of problems addressed in this study(18-21). Articles related to different aspects of this study and cardiovascular investigations were reported (22-25).

References:

1. Dalal PM. Cerebrovascular Disorders API textbook of Medicine 11th edition 1401-10
2. Anand K, Chowdhury D, Singh KB, Pandar CS. Estimation of mortality due to stroke in India. Neuroepidemiology 2001;20:208-11
3. Cropp D, Manning GW. ECG changes simulating myocardial ischemia and infarction associated with spontaneous intracerebral hemorrhage. Circulation 1980;12:25
4. Incidence and Pattern of ECG Changes in Patient with Cerebrovascular Accidents: An Observationa lStudy :Arohi Kumar Indian Journal of Basic & applied medical research ; March 2015:Vol4,Issue2,P.617-621.
5. Arab, D., Vahia, AM, Qureshi, AI. Cardiovascular manifestation of acute intracranial lesions; pathophysiology, manifestation and treatment. J intensive care med ;2003;18:119-29
6. A. P. S. Tomar, Satish K. Ramteke, Ravita Singh, Sharmila Ramteke. “Study of ECG and echocardiographic abnormalities in Stroke Patients and its Prognostic Significance”. Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 11, March 17; Page: 2693-2698
7. KR, Geld AW, Mannien PH, Boughner DR, Bisnaire D . Cardiac function in aneurysmal SAH – A study of Electrocardiographic and Echocardiographic abnormalities. British Journal of Anaesthesia 1991 Jul; 67(1):58-63
8. Sakka SG, Haettemann E, Renhart K . Acute left ventricular dysfunction and Subarachnoid Hemorrhage. J. Neurosurg. Anesthesiol 1999 Jul;11(3):209-13
9. The cardiac diagnostic work-up in stroke patients—A subanalysis of the Find- AF RANDOMISED trial Katrin W Wasser, Mark Weber-Kru¨ger2, Falko Ju¨rries2, Jan Liman1, Gerhard F. Hamann3 ,Pawel Kermer4 2019
10. Ruth Bontia. Epidemiology of stroke. Lancet 1992; Vol 339;343-4
11. Khechinashvili G, Asplund K. Electrocardiographic changes in patients with acute stroke: a systematic review. Cerebrovasc Dis. 2002;14(2):67-76
12. Bozluolcay et al. Electrocardiographic findings and prognosis in Ischemic Stroke. Neurology India 2003; 51(4): 500-502.\
13. Hanne Christensen. Abnormalities on ECG and Telemetry predict Stroke outcome at three months. Journal of the Neurological Science 234(2005) 99-103.
14. Jane G Morris MD: E. Jesus Duffis, MD. Cardiac Work Up of Ischemic Stroke. Stroke. 2009; 40: 28932898.
15. Tiago Tribolet de Abreu, MD et al –Therapy Implications of Transthorasic Echocardiography in Acute Ischaemic Stroke Patients.

16. Ramon Pujadas Capmany et el : Specific cardiac disorders in 402 consecutive patients with ischemic cardioembolic stroke. International Journal of Cardiology 95 (2004) 129-134.
17. Nishide M, Irino T, Gotoh M, Naka M, Tsuji K. Cardiac abnormalities in ischemic cerebrovascular disease studied by two-dimensional echocardiography. Stroke. 1983 Jul;14(4):541-5.
18. James, Spencer L, Chris D Castle, Zachary V Dingels, Jack T Fox, Erin B Hamilton, Zichen Liu, Nicholas L S Roberts, et al. "Estimating Global Injuries Morbidity and Mortality: Methods and Data Used in the Global Burden of Disease 2017 Study." *Injury Prevention* 26, no. Supp 1 (October 2020): i125–53. https://doi.org/10.1136/injuryprev-2019-043531.
19. Murray, Christopher J L, Cristiana Abbafati, Kaja M Abbas, Mohammad Abbasi, Mohsen Abbasi-Kangevari, Foad Abd-Allah, Mohammad Abdollahi, et al. "Five Insights from the Global Burden of Disease Study 2019." *The Lancet* 396, no. 10258 (October 2020): 1135–59. https://doi.org/10.1016/S0140-6736(20)31404-5.
20. Khanna, S., A. Inamdar, S. Kumar, and A.V. Basat. "Study of Serum Uric Acid Levels in Acute Stroke." *International Journal of Pharmaceutical Research* 11, no. 4 (2019): 2041–44. https://doi.org/10.31838/ijpr/2019.11.04.508.
21. Bawiskar, N., N. Kothari, S. Kumar, S. Acharya, and S.S. Chaudhari. "Clinico-Radiological Association of Serum Calcium, Ionic Calcium and Albumin Corrected Serum Calcium in Acute Ischaemic Stroke." *International Journal of Pharmaceutical Research* 11, no. 3 (2019): 1445–48. https://doi.org/10.31838/ijpr/2019.11.03.159.
22. Sahu, A., and W.M. Naqvi. "Upper Limb Functional Independence in Subacute Stroke Patients: A Study Protocol Investigating the Impact of Haptic Enhanced Virtual Reality System." Journal of Critical Reviews 7, no. 9 (2020): 446–51. https://doi.org/10.31838/jcr.07.09.91.
23. Sagar, V., A. Wanjari, S. Kumar, and A.P. Munshi. "Echocardiographic Assessment in Various Obesity Phenotypes." *International Journal of Pharmaceutical Research* 11, no. 2 (2019): 1804–7. https://doi.org/10.31838/ijpr/2019.11.02.201.
24. Choudhari, M.S., N. Charan, M.I. Sonkusale, and R.A. Deshpande. "Inadvertent Diversion of Inferior Vena Cava to Left Atrium after Repair of Atrial Septal Defect - Early Diagnosis and Correction of Error: Role of Intraoperative Transesophageal Echocardiography." Annals of Cardiac Anaesthesia 20, no. 4 (2017): 481–82. https://doi.org/10.4103/aca.ACA_83_17.
25. Schwartz, G.G., P.G. Steg, M. Szarek, D.L. Bhatt, V.A. Bittner, R. Diaz, J.M. Edelberg, et al. "Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome." New England Journal of Medicine 379, no. 22 (2018): 2097–2107. https://doi.org/10.1056/NEJMoa1801174.