CONFERENCE PROCEEDING

Heart in the brain injured

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INTRODUCTION

Normal functioning brain has an important role in controlling the heart and lung functions. The process of control of these organs by the brain is through neural as well as hormonal mechanisms. Neural control occurs by the autonomic nervous systems, and the hormonal control occurs using various mediators such as norepinephrine. Various centres are located in the brain that affect the functions of the heart. Hence, it is understood that any injury of moderate to severe nature will affect the cardiopulmonary functions. Studies have shown that damage to the heart and lung are independent predictors of mortality in brain injured patients. This review will explain the various pathological processes involved in the damage to the heart due to acute brain injury.

BRAIN-HEART INTERACTIONS

Brain plays a crucial role in the control of the heart. However, the interaction between these two structures is a complex phenomenon. The interactions can be classified into three ways (1) effects of cardiac dysfunction on the brain (as in stroke or low cardiac output) (2) effects of brain injury on the heart (3) combined neuro cardiac syndromes.[1]

Sudden cardiac arrest caused by acute emotional disturbance (such as fear and bereavement) raised lots of interest in the control of the brain over heart. Initially, it was thought that the sudden sympathetic surge from the brain following emotional distress caused severe intractable arrhythmias of the heart and caused death or myocardial damage. The primary areas responsible for the interaction were found to be in the insular region and limbic system (amygdala and hippocampus). Following this, animal experiments showed that excessive activity of the parasympathetic system also played role in the myocardial damage. The current understanding is in massive stress causes an autonomic storm. In the immediate period, it activates the sympathetic system and in the later stages the parasympathetic system; both are thought to be responsible for the myocardial dysfunction seen in these patients.[1] In addition, it was recognised that the cerebral hemispherical dominance with regard to autonomic control (right predominantly sympathetic and left predominantly parasympathetic) probably also contributes to the dominant mechanism of sudden death (i.e., sympathetic vs. vagal).[2]

CENTRAL REGULATION OF THE AUTONOMIC NERVOUS SYSTEM

The autonomic nervous system consists of complex network of structures present in the central nervous system (CNS). The organisation of the central network and its function are:[3]

- Spinal system: Segmental sympathetic or sacral parasympathetic-concerned with local reflexes
- Bulbopontine network: Reflex control of circulation and respiration
- Pontomesencephalic network controls the pain modulation and response to stress
- Frontal lobe network includes hypothalamus, limbic systems (including insula); controls the emotional response to stress, endocrine and haemodynamic homeostasis.

Acute stroke and cardiac dysfunction

Cardiac dysfunction is a well-known accomplishment of patients presenting with acute stroke. Extensive research has helped us in understanding the pathophysiological mechanisms, anatomical correlates responsible for cardiac dysfunction.

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It has been well documented that in patients presenting with acute stroke, there is associated cardiovascular dysfunction. A large body of data exist in patients with acute ischemic stroke; however cardiac complications have been documented in the haemorrhagic stroke patients as well. The overall mechanism and pathophysiology between the two conditions are similar. This can adversely affect the outcome of these patients. The cardiovascular changes described commonly are the electrocardiogram (ECG) changes such as arrhythmias, QT prolongation and T wave inversion.[4] Elevated troponin T have also been demonstrated in studies indicating myocardial damage. The risk of sudden cardiac death from acute stroke is approximately 2% to 6%.[5] The changes have been thought to be due to imbalance in the autonomic balance.[6] Right-sided stroke patients have been found to have more cardiac dysfunction.[7]

The analysis of heart rate variability (HRV) is known to provide useful information about disturbances in autonomic regulation in several cardiac affections. It is a reflection of the amount of heart rate fluctuation around the mean heart rate and reflects the balance between the sympathetic and parasympathetic nervous systems. HRV is done by analysis of changes in R-R intervals in Holter monitoring. Frequency analysis of the changes in R-R intervals using fast Fourier analysis produces power spectrum from the 0.01-Hz to 1.0-Hz unit. Three frequency domain measures of HRV, including low-frequency (LF) (range, 0.04–0.15 Hz), high-frequency (HF) (range, 0.15–0.40 Hz) and LF/HF ratio, were calculated. HF component of HRV correlate with respiratory rhythm and have generally been considered as measures of parasympathetic tone, whereas the LF component correlates with peripheral vasomotor activity and thermoregulation, representing both parasympathetic and sympathetic influences. LF/HF ratio appears to be an accurate marker of the shifts in sympathovagal balance.[8]

In a study on stroke patients using HRV, Colivicchi *et al*. have found that decrease in HRV was found in right insular stroke patients indicating a disturbance in the autonomic function.[9] They also found that patients with right-sided insular damage showed significantly more premature ventricular arrhythmia and premature supra-ventricular contractions than patients with left-sided infarctions and a significantly higher prevalence of both non-sustained ventricular tachycardia and supra-ventricular tachyarrhythmias than all other stroke subgroups. Abnormal long-term HRV measure power-law slope β, an exponent that reflects an altered distribution of spectral characteristics over ultra-frequency and very LF bands, was the best univariate predictor of death.

Blood pressure variability

Alteration in the autonomic nervous system (ANS) during acute phase of stroke has been found to cause impaired blood pressure (BP) control in the first few days. There can be severely elevated BP caused by elevated levels of circulating norepinephrine, dopamine.[10] The increase in BP usually returns to baseline at 7 days post-stroke. The increase has been found to be higher with hemispheric stroke compared to lacunar stroke. Each 0.1 mmHg/min increase in the 24-h rate of systolic BP variation was associated with a 1.96-fold increase in the odds of a negative outcome.[11]

It has also been found that the autonomic dysfunction persisted in large infarcts for several months causing flotation in the BP values.

Baroreflex sensitivity variability

Baroreceptor sensitivity has also been found to be altered in acute stroke but less well studied compared to HRV. Neural afferents from these baroreceptors relay information to the nucleus tractus solitarius and the ventrolateral medulla, which is further processed in the insula, medial prefrontal cortex, cingulate cortex, amygdala, hypothalamus, thalamus and cerebellum.[12] Changes in baroreceptor sensitivity are responsible for swings of BP variation in acute stroke. It has also been found to affect the prognosis.

Location of stroke and cardiac dysfunction

Acute large strokes produce major cardiac dysfunction compared to lacunar strokes. Certain locations of the stroke are also found to have increased predilection for cardiac dysfunction. Right insular stroke or right middle cerebral artery stroke, parietal lobe as well as frontal lobe stroke have all been implicated in onset of cardiac dysfunction, arrhythmias and sudden death in different studies. Attempts are being made to increase the parasympathetic activity using vagal nerve stimulation in order to counter the ill effects of the imbalance caused by the sympathetic nervous system. Some experiments have found this beneficial in terms of neuroprotection reducing inflammatory and immunological adverts effects.[13]

OTHER NEUROLOGICAL CONDITIONS

Cardiac dysfunctions have been described in acute neurological illness, mainly consists of ECG changes. Various conditions that can impact the cardiac function include status epileptics, coma, neurocritical care patients with neuromuscular disorders, meningitis and electrolyte imbalances.

CARDIAC DYSFUNCTION IN HEAD INJURED

Traumatic brain injury (TBI) is one of the leading causes of disability and death in the world. The effects of the

brain injury on the cardiac dysfunction have been of considerable interest in the recent times. Cardiac dysfunction following TBI can adversely affect the outcome of the patients.

ECG analysis of patients with TBI have shown prolongation of the QT interval, ST segment abnormalities, flat or inverted T waves, U waves, peaked T waves, Q waves and widened QRS complexes. Prolongation of QT interval has been associated with severity of injury and can precipitate ventricular arrhythmias.[14]

In a retrospective analysis of TBI patients, Prathep *et al*. found that 22% of patients had echocardiographic evidence of cardiac dysfunction within 2 weeks of the head injury. The commonly observed abnormalities include low ejection fraction, regional wall motion abnormalities (RWMA). The cardiac dysfunction was found to be independent predictor of in-hospital mortality.[15] The possible mechanisms of cardiac dysfunction are due to excess catecholamine surge causing myocardial damage. Various causes have been implicated in the catecholamine surges which include initial injury, raised intracranial pressure, cerebral injury, hypothalamic injury and neuro-inflammation. This was supported by elevation of cardiac enzymes such as creatine phosphokinase-MB and troponin-I. The authors have suggested that patients with age ≥65 years, elevated cardiac enzymes (creatine kinase-MB and troponin I), and head abbreviated injury scale 4–6 can be used to predict cardiac dysfunction in head injured patients.

There are limited data on the prevention and treatment of cardiac injury in TBI patients. It is important to recognise the cardiac complications and manage the patient accordingly.

CARDIAC DYSFUNCTION IN SUBARACHNOID HAEMORRHAGE

Extensive literature exists on the myocardial dysfunction in subarachnoid haemorrhage (SAH) patients. SAH produces the most severe forms of cardiac dysfunctions. Though non-aneurysmal SAH can also lead to myocardial damage, aneurysmal SAH has higher incidence as well as more severe form of dysfunction. ECG changes, in the form of T-wave inversion and QT interval prolongation, has been found in 50–100% of patients, troponin elevation is seen in 20–40%, and RWMA occur in 10% of aneurysmal SAH.[16,17] In a large study, Kim *et al*. have found that incidence of cardiac failure in 6.7% and myocardial infarction (MI) in 0.28% of aneurysmal SAH. Moreover, patients with cardiac dysfunction also had more mortality.[18] Fatal arrhythmias have been reported. The mechanism behind the development of cardiac dysfunction is postulated to be catecholamine storm following SAH. The cardiac dysfunction in SAH can be a varied spectrum from mild to severe. The severity of the dysfunction depends on various factors including age and severe grading of SAH co-existing conditions.[18] Mild dysfunction consists of ECG changes. Severe dysfunction can cause two types of dysfunction:

a. Neurogenic stunned myocardium
b. Stress cardiomyopathy.

Neurogenic stunned myocardium

Neurogenic stunned myocardium occurs in 20% of SAH patients. The pattern of neurogenic stunned myocardium includes ECG changes (T wave inversion, QT prolongation, ST-T changes). Elevated troponin I can be present in 20% of patients. Patients can present with either cardiac failure or features resembling MI. Echocardiography usually reveals left ventricle (LV) dysfunction in the form of low ejection fraction, RWMA, especially in the apical region. The differentiation from MI is usually by the varied pattern of RWMA not relating to a particular coronary artery territory, and the elevation of cardiac enzymes is less pronounced than that seen in MI.[19] The main theories involved in the development includes coronary vasospasm, microvascular dysfunction of catecholamine-induced myocardial damage. The clinical features start within 48 h and last for a week. Elevated brain natriuretic peptide and troponin may identify patients at risk for neurocutaneous melanocytosis. However, many of the patients will require hemodynamic support and have increased mortality.[20]

Stress cardiomyopathy

It is another form of severe cardiac dysfunction that occurs infrequently in aneurysmal SAH patients. It is also called as Takatsubo cardiomyopathy. The characteristic feature is the apical ballooning of the LV. It is not specific to SAH as it is seen in other CNS diseases all well. The salient diagnostic features of tako-tsubo cardiomyopathy include reversible wall motion abnormalities at the LV apex and/or mid-ventricle, extending beyond a single coronary artery distribution; T wave and ST segment abnormalities on ECG; minor elevation in cardiac markers; and the absence of significant coronary artery disease.

REVISED CRITERIA FOR THE DIAGNOSIS OF TAKO-TSUBO CARDIOMYOPATHY PROPOSED BY MAYO CLINIC

Each and every criterion should be met for a reliable diagnosis of apical ballooning syndrome:

- Transient hypokinesia, akinesia or dyskinesia of the left ventricular mid-segments with or without apical involvement RWMA extend beyond a single epicardial vascular distribution; a stressful trigger is often but not always present

- Absence of obstructive coronary disease or angiographic evidence of acute plaque rupture
- New ECG abnormalities (either ST-segment elevation and/or T-wave inversion) or modest elevation in cardiac troponin
- Absence of pheochromocytoma myocarditis.

The prognosis is usually good in many cases as it is a self-limiting disease.[20]

The characteristic histological features of myocardial damage produced in SAH consist of contraction band necrosis in contrast to MI where coagulation necrosis is seen.[20] The aetiology for these changes was thought to be the local release of catecholamine from myocardial sympathetic nerve endings.[21]

CONCLUSION

Cardiac dysfunction is common in many neurological and neurosurgical condition. The basic pathological mechanism responsible for the dysfunction appears to be the imbalance in the autonomic function due to the loss of control by the brain. Studies have shown that cardiac dysfunction affects the overall outcome of the patients in the form of increased hospital stay and mortality. The mainstay lies in the recognition by standard monitoring, differentiating from the organic cardiac cause. There is a limited literature on the specific management issues. Most of the patients undergo supportive management only.

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Conflicts of interest
There are no conflicts of interest.

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