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Understanding the underlying pathophysiology mechanisms and therapeutic approach towards the stroke

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Abstract
Stroke is the type of neurological disorders, which cause a major impact all over world and also consequences to death. Several key mechanism such as oxidative stress, failure of energy, necrosis and excitotoxicity etc involved in such kind of disorder. It is complex disorders, which includes ionic imbalance, neuriprotection, cell death. Several therapeutic approach towards the management of stroke, which based on cerebral flow and ultimately reduced the risk factors of ischemia. Throughout understanding the pathophysiological mechanism and used appropriate measure of prevention, can be basis for the effective treatment strategies for prevention of stroke. This review paper highlights the pathophysiological mechanism and therapeutic approach towards the stroke.

Keywords: Stroke, excitotoxicity, oxidative damage, apoptosis

Introduction
Stroke, is a neurological disorders, which may consequences of defective cerebral blood flow. Stroke is main causing factor of death all over the world and is also main basis for morbidity, generally in aged or middle aged peoples (Adams *et al*., 2007; Adibhatla and Hatcher, 2008; Baidya *et al*., 2013; Bakhai *et al*., 2004) [1, 2, 3, 4]. Women are more affected by stroke. Rapid failure of functions of brain, which may be due to interruption in supply of blood to parts of brain. Stroke has a major impact on community, which may be enlarge in future (Bath *et al*., 2000; Beamer *et al*., 1995; Adams *et al*., 2007; Adibhatla and Hatcher, 2008; Benveniste, 2009) [5, 6, 7, 1, 2]. Stroke is an complex pathophysiology mechanism, which several key mechanism like oxidative stress, ionic imbalance, neuroprotection and various inflammatory mechanism involved in pathophysiology of stroke. This leads to impaired functions of neuron, which may consequences of ischemic. On focusing the cerebral flow and reduced the toxic effects in case of ischemia, the therapeutic management can be achieved (Bhatti *et al*., 2013; Bruijn *et al*., 1999; Caplan, 2017) [8, 9, 10].
Hypertension, diabetes mellitus are the main risk factors of this complex disease. Several study indicate that pregnency, hormonal therapy may increased the risk of this disease. Ischemia and the infraction, which are the consequences of artherosclerotic growth of emboli and thrombi. Generally a clot interruption occurred within the blood vessel and the blood is not able to reach to brain' parts. Due to these interruptions of blood flow in blood vessel, the cell of brain initiate to die and stroke may occurred. Weakness of body parts such as legs and arms are the consequences of small stroke and higher degree of stroke leads to caused paralysis and loss of speech (Chan, 2001; Christophe and Nicolas, 2006) [11, 12]. This review paper highlights the clinical signs and symptoms of stroke, main types of stroke, complication, pathophysiological mechanism and preventive measure towards the stroke.

Types of stroke
Ischemic and Hemorrhagic are the main types of stroke. Thrombotic stroke and Embolic stroke are subtypes of Ischemic stroke and Intracerebral hemorrhage, Subarachnoid hemorrhage and Transient ischemic attack (TIA) are the types of hemorrhagic stroke (Degterev *et al*., 2005; Denes *et al*., 2010; Eliasson *et al*., 1997; Emsley *et al*., 2002) [13, 14, 15, 16]. The various types of stroke are presented in figure-2.

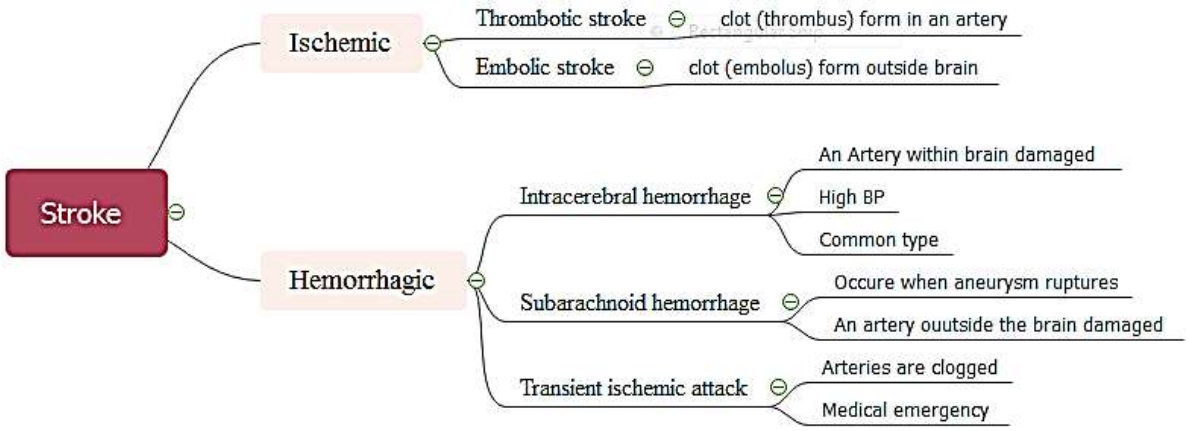

Fig 1: Types of stroke

Clinical signs and symptoms of stroke

Several clinical features of stroke are summarized in figure no-2 (Emsley *et al*., 2002; Hickenbottom and Barsan, 2000; Imai *et al*., 2003) [16, 29, 31]

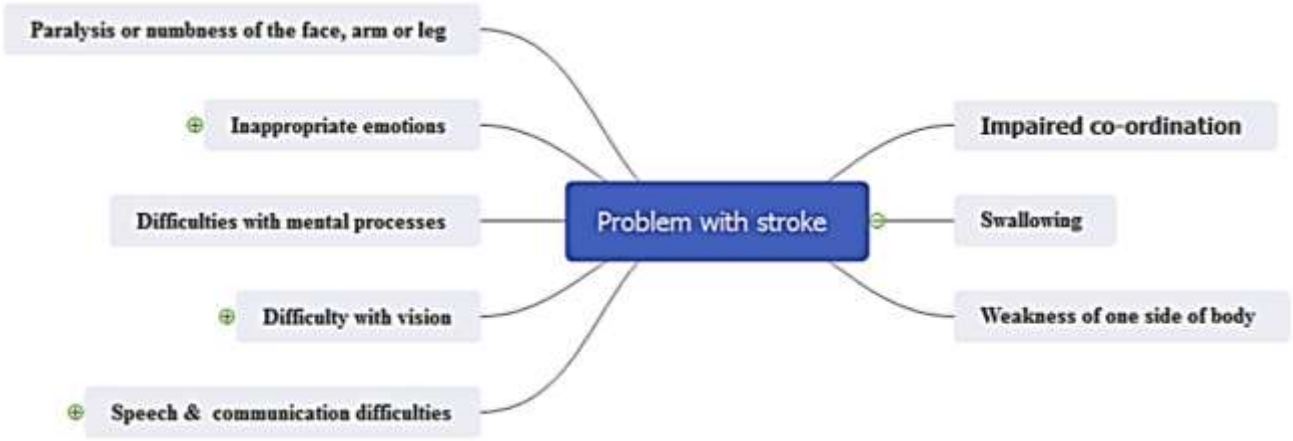

Fig 2: Clinical symptoms of Stroke

Complications

Several complication of stroke are summarized in figure- 3 (Escudero Aug, *et al*., 2008 ; Caplan, 2017; Furie *et al*., 2017; Emsley *et al*., 2002; Escudero *et al*., 2008) [16, 17, 10].

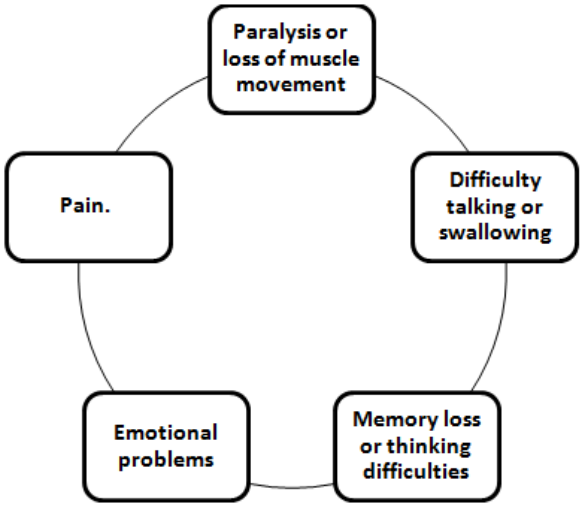

Fig 3: Complications of stroke

Pathophysiology mechanism involved in stroke

In brain, there is rapid blockade in blood flow, which consequences to collapse the process such as hemodynamic, metabolic and biochemical. Several mechanism overload of calcium, excitotoxicity, dysfunction of mitochondria, inflammatory processes stress on endoplasmic reticulum and oxidative stress (Mehta, *et al*., 2014; Feigin and Krishnamurthi, 2016; Ferrer *et al*., 2013) [18, 19, 36].

Due to sudden interruption in the blood flow to cascade to brain, which leads to deprive the brain tissue for supply of glucose and oxygen. Stroke is leading factor of death all over the world and approximately 15 million persons suffering from this disease (Mehta, *et al*., 2014; Feigin and Krishnamurthi, 2016; Ferrer *et al*., 2013; Glykys and Mody, 2006) [18, 19, 20, 21, 36].

Glutamate release, calcium influx, homeostatic imbalance and depolarization, phospholipases and proteases (calcium sensitive enzymymes), free radical formation, oxidative stress, apoptosis, necrosis, cytochrome C release, activation of Capase - 9 and damage of DNA are main key factors, which are basis of therapeutic approach of stroke (Graham *et al*., 2001; Grau *et al*., 2001; Gudlavalleti *et al*., 2015; Heiss *et al*., 1999; Hermann *et al*. 2001; Heuschmann *et al*., 2003) [22, 23, 24, 25, 27, 28].

Inflammatory mechanism in the stroke

In recent study targets that several inflammatory processes involved in progression of this severely illness. It is linked with several disease, which are summarized in figure-2 (Jin *et al*., 2010; Hu *et al*., 2000; Emsley *et al*., 2002; Hickenbottom and Barsan, 2000; Imai *et al*., 2003) [16, 29, 31, 32].

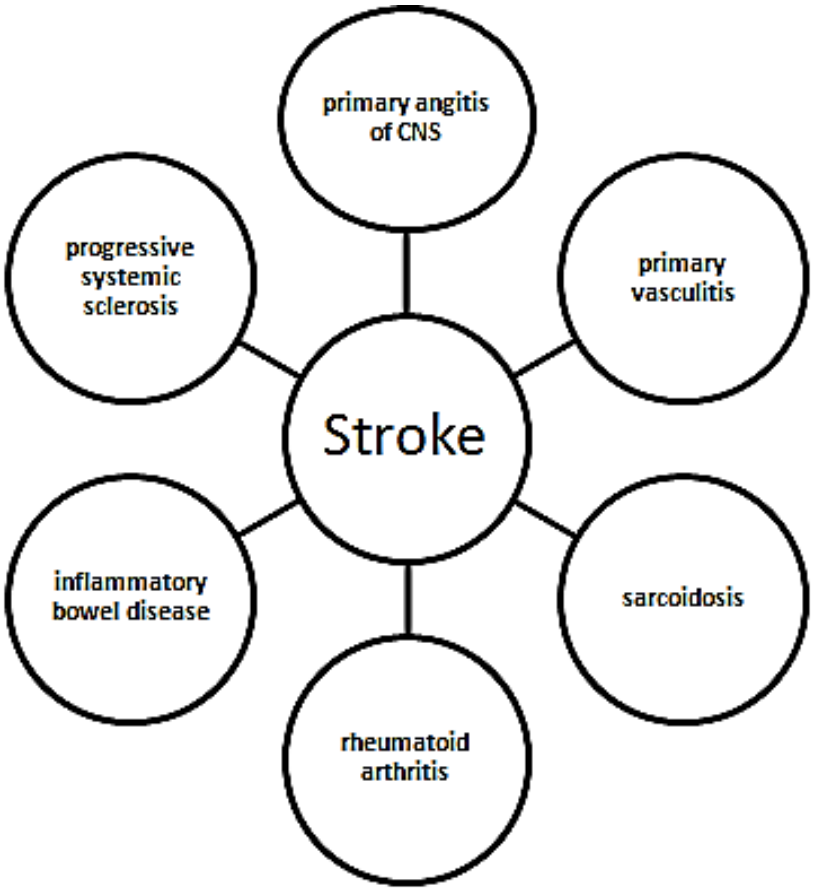

Fig 4: Associated conditions with Stroke

Inflammation processes, production of nitric oxide, apoptosis and free radical damage are the process, which participate in mechanism of tissue injury of ischemic type cascade. In such type, cell signaling of temporal changes, transduction of signal, several gene regulation and its expression are the consequences of brain ischemia. Several therapeutic targets to reduce the loss of tissue and defect in neurological (Adibhatla *et al*., 2008; Mehta *et al*., 2009; Tanaseseu *et al*., 2008; Krupinski *et al*., 2000; Lee *et al*., 2014; Nakka *et al*., 2008; Niizuma *et al*., 2010; Oliveira-Filho, 2017) [2, 33, 35, 36, 37].

5.2 Role of Cytokine in Stroke

In acute brain injuries and ischemic type, inflammation process play a wide role in pathogenesis mechanism. Cytokines such as interlukin (IL-1and IL-6), TNF of α and β, adhesion molecules like integrins, selectins and immune-globulins, nitric oxide synthease and eicasanoids are involved in inflammatory mechanism, which are represented in figure - 4. (Jin *et al*., 2010; Oliveira-Filho, 2017; Rodrigo *et al*., 2013) [32, 39, 40].

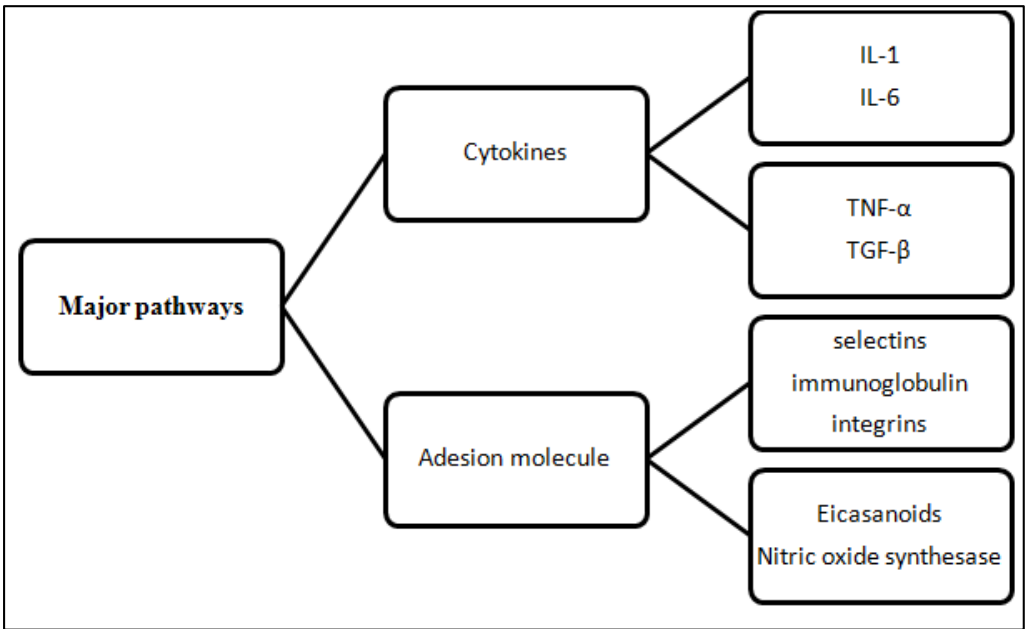

Fig 5: Main cascade involved in inflammatory process

The inflammatory process after intitation, which leads to irreversible damage the function of brain and a interplay involved between the mechanism of astrocytes, leukocytes, endothelial and microglial cells. Leukocyte infiltration, MAPKS dependent signaling and antioxidant are basis of therapeutic approach for stroke, which may improve the outcome and also minimize the impaired functions of brain (Deb *et al*., 2010). Polyypeptides linked with activation of immune, inflammatory process and cell death or cell differentiation. Several cytokine such as TNF-alpha and IL-1 damaged the parenchymal cell and IL-10, IL-1 of receptor inhibitors, which play a major role as neuroprotective and antinflmmatory respone (Emsley *et al*., 2002; Adibhatla *et al*., 2008; Beamer *et al*., 1999; Stout *et al*., 1998; Warner *et al*., 2004; Zanchin *et al*., 1995) [16, 2, 6, 32, 41, 42, 43].

Preventive approach towards the stroke

Several approaches to prevent this such kind of complex heart disease are as summarized in figure -4 (Escudero *et al*., 2008; Caplan, 2017; Furie, 2017) [17, 10]:

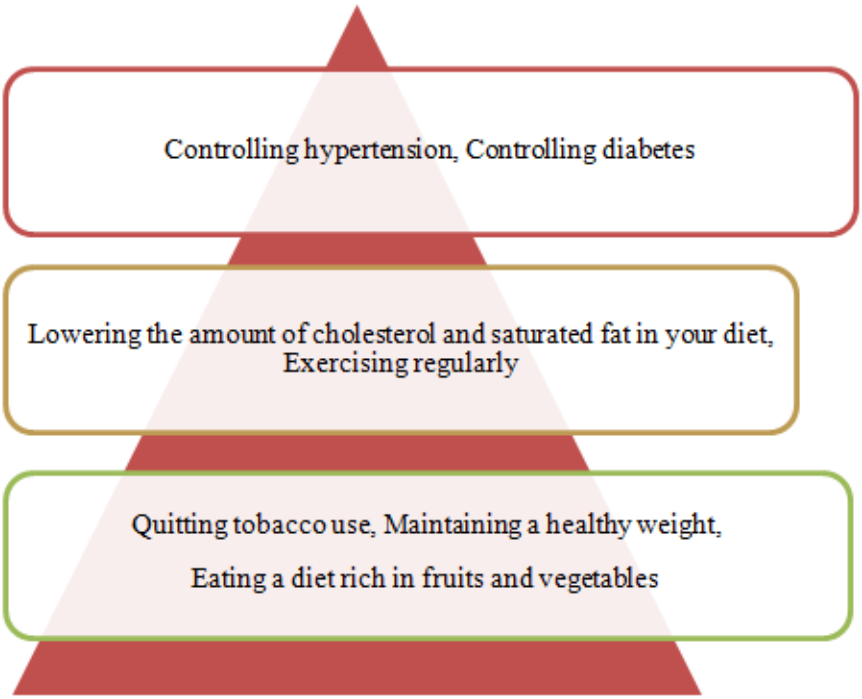

Fig 6: Prevention approaches towards stroke.

Conclusion

Stroke is an condition in which several mechanism (failure of energy, oxidative stress, cell death, excitotoxicity etc. play a major role in pathophysiological mechanism. Several factors such as hypertension, diabetes mellitus and arthrosclerosis are causing risk factors of stroke. Due to irreversible impaired the function of brain and impaired the neuronal functions leads to this complex illness. Through understanding the main mechamism such as inflammatory process are the basis of therapeutic approach of this complex disease. Early detection and prevention may minimize the risk and also manage the complications of stroke, which may ultimately leads to cure such kind of disease.

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