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Identification and assessment of Modifiable and Non-Modifiable risk factors and oxidative stress in pathophysiology of stroke diseases- a review

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Abstract.

The aim of this review is the identifying the main factors risk factors and manifesting the role of oxidative stress as factors associated with stroke diseases. It is very difficult to determine the cause of stroke but studies scientists have shown that some characteristics and non-modifiable factors of peoples played a major role in developing stroke like, age, Gender, Race and Heredity. Other modifiable risk factors include hypertension, Heart disease, Diabetes mellitus, Dyslipidemia and Obesity have also been associated with higher stroke incidence. On the other hand, studies support that oxidative stress is directly involved in the genesis and aggressiveness appearance of stroke. However, cerebral dysfunction like ischaemia would be followed by reperfusion leads to increased production of free radicals which induce also oxidative stress. In conclusion, changing human behavior in life is the first way to prevent stroke disease; on the other hand, we suggest that antioxidants treatment has great benefits in improving patient health and decreasing the vascular complications of stroke.

Keywords: Stroke, risk factors, oxidative stress, antioxidants.

Introduction

The brain is Despite representing only an extremely energy demanding organ .˷2% of body mass, it consumes˷ 20% of the total energy in a resting state[1]. An adequate blood supply is instrumental to normal brain functioning. The brain's vasculature is composed of a complex

network of arterioles, capillaries, venules, and veins that regulate cerebral blood flow (CBF) and maintain the integrity of the blood brain barrier (BBB) [2]. The brain is vascularized by 4 main arteries; internal carotid arteries and arteries right and left vertebral. The two carotid arteries form the anterior circulation, the vertebral arteries when they unite in a basilar trunk thus forming the circulation posterior [3,4]. The internal carotid arteries originating from the common carotid arteries, and the vertebral arteries. They form the Circle of Willis at the base of the brain, from which the main cerebral arteries are advancing and branching at the surface of the brain [5]. Brain diseases including cerebrovascular accident are globally challenging issues [6]. Cerebrovascular accident (Stroke) is a disease that affects the system of brain vasculature [7], defined as a clinical picture of vascular origin and a focal neurological deficit [8] (burst of cerebral arteries , hemorrhage , or occlusion by o thrombus or other particles) leading to cerebral dysfunction [9], this deficit characterized by the rapidity of symptom resolution (within 24 h) , with or without demonstrable new hemorrhage or infraction in the brain [10]. Many of recent landmarks in scientific research have shown that in human beings, Oxidative stress is an important factor causing metabolic and physiological alterations and various diseases in the body [11], it is as a consequence of increase a reactive oxygen species and decrease in antioxidant defenses in prevalent in many health problems [12].In light of these data, the aim of this review is to identify the major risk factors and the role of oxidative stress as factors associated with stroke diseases.

Ischemic stroke

Ischemic stroke is the most prevalent type of stroke [13]. Defined as neurological event, characterized by a sudden lack or complete interruption of blood flow in a brain supplying artery by a thrombus or embolus and reduces oxygen and energy supply to the critical tissues of the brain resulting in rapid cell death and cones ponding loss of neurological function [14].The TOAST classification1 defines 5 IS subtypes based on etiology: 1) large-artery atherosclerosis, 2) cardio embolism, 3) small-artery occlusion, 4) stroke of other determined etiology, and 5) stroke of undetermined etiology [15].The event resulting from any subtypes of ischemic stroke result in the loss of blood supply , oxygen , nutrients and elimination of metabolic wastes [16]. Neuronal death in ischemia occurs through apoptosis, necrosis, and autophagy after changes obstruct normal neuronal functioning such as ATP depletion and loss of ion exchange function of membrane pumps, terminal depolarization and glutamate mediated calcium excite toxicity, calcium dependent enzyme activation, generation of free radicals, and ultimately degradation of

cellular molecules[17].A middle cerebral artery (MCA) stroke (figure 1) occurs when the middle cerebral artery, which supplies the frontal lobe and lateral surface of the temporal and parietal lobes with blood, becomes blocked[18].

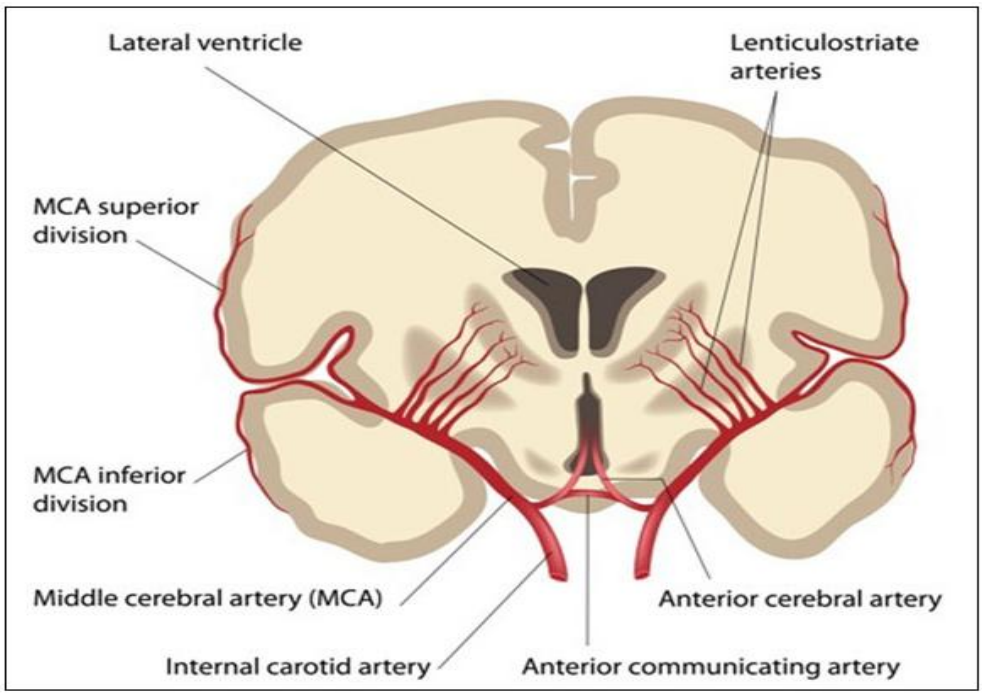

Figure 1: A middle cerebral artery stroke[18]

Hemorrhagic stroke

Hemorrhagic strokes due to an abnormal vascular structure or the rupture of a blood vessel, including two main types intra cerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH) [19]. ICH refers to bleeding within the brain itself, while SAH refers to bleeding that occurs outside of the brain tissue but still within the skull, precisely between the arachnoid mater and pia mater. The pressure of the blood causes brain tissue death(figure 2)[20].Intra hemorrhage (ICH) is usually caused by rupture of small penetrating arteries secondary to hypertensive change or other vascular abnormalities[21]. Its pathophysiology consists of three distinct phases: (1) initial hemorrhage, (2) hematoma expansion and (3) peri hematoma edema[22].

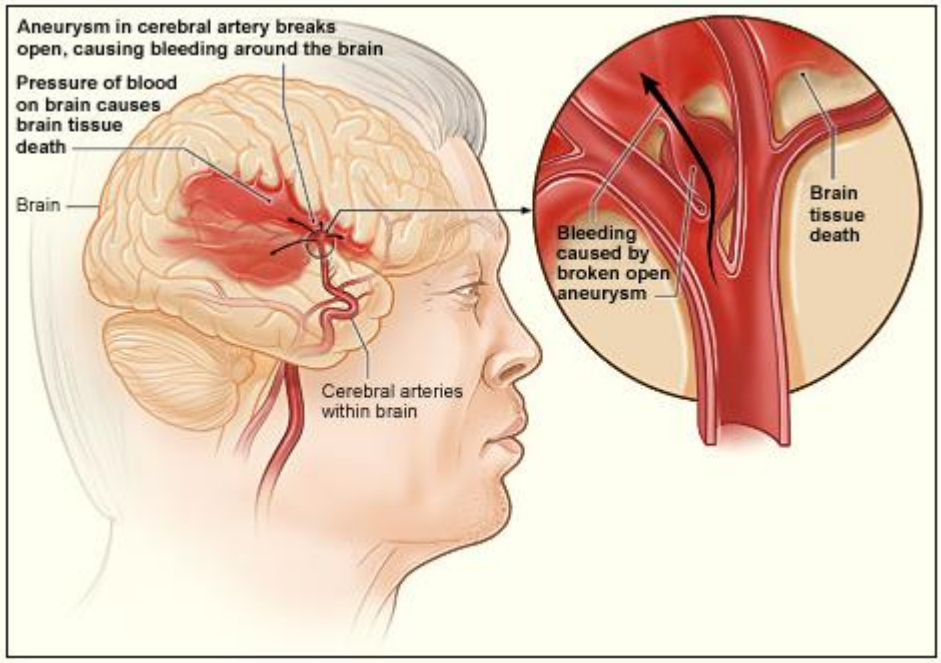

Figure 2:Hemorrhagic stroke in the brain[20].

The initial injury mechanism in ICH is compressing brain parenchyma by hematoma 's mass effect, resulting in physical disruption of parenchymal architecture [23] in contrast a secondary mechanism of brain injury is related to clotting cascade after endothelial damage and hemoglobin breakdown [24].The pathophysiology of SAH is complicated and includes vasospasm (VS), micro-circulatory dysfunction, neuronal apoptosis [20].

Risk factors of stroke

Risk factors are certain characteristic that give an increase likelihood of having stroke [25]. Risk factors for hemorrhagic and ischemic stroke are similar, but there are some notable differences [26].Lifestyle plays an important role in the etiology of this disease, including diet [27]. Risk factors for stroke are usually divided into non modifiable including age, Gender, Race and Heredity and modifiable such as hypertension, Heart disease, Diabetes mellitus, Dyslipidemia, Obesity, Smoking, Excess alcohol consumption [28].

Non-Modifiable risk factors

For each consecutive decade after 55 years of age, the risk for stroke approximately doubles. The prevalence of stroke for individuals older than 80 years of age is approximately 27%, compared with 13% for individuals 60 to 79 years of age. In general, stroke is more

prevalent in men than in women. The incidence of stroke in the young (aged 35–44) is highest in women, however. The increased risk associated with pregnancy is most significant postpartum [29].In relation to race/ethnicity, African-Americans and some Hispanic/Latino American groups have a higher incidence and mortality of stroke. Prevalence and severity of risk factors and markers such as hypertension, diabetes, and obesity have been used to explain, at least in part, these disparities in stroke rates. Also, social determinants may play an important role [30].Genetic factors that may be associated with stroke include family history of stroke, a number of inherited autosomal-dominant trait coagulopathies (eg, protein C and S deficiencies). There are many other genetic conditions (eg, inherited metabolic disorders, certain intracranial aneurysm alleles and mutations in the amyloid precursor protein genes causing inherited cerebral amyloid angiopathy syndromes) [30].

Modifiable risk factors

Hypertension is the most important modifiable risk factor for stroke, with a strong, direct, linear, and continuous relationship between blood pressure and stroke risk. Heart diseases such as; A trial fibrillation (AF) has long been recognized to be a major risk factor for stroke, and this has only increased with the aging of the US population [26]. The Utilization of long-term anticoagulation therapy in the treatment of AF patients significantly increases the risk of future intra cerebral hemorrhage (ICH)[31].Diabetes is an independent risk factor for stroke disease Compared with patients without, patients with diabetes have at least twice the risk for stroke, and approximately 20% of patients with diabetes will die from stroke [32].The relationship between dyslipidemia and stroke risk is complex, with an increased risk for ischemic stroke with increased total cholesterol, and a decreased risk for ischemic stroke with elevated HDL cholesterol. Total cholesterol, meanwhile, is inversely associated with hemorrhagic stroke, with hemorrhagic stroke risk increasing as total cholesterol decreases [26].Obesity is an established risk factor for the development of vascular diseases such as stroke [33]. It has classically been associated with disruption of pathways controlling lipid and glucose metabolism, however recent evidence has shown that obesity also has an inflammatory component, which is well established factor in stroke risk and outcome [34].Cigarette smoking is a causal risk factor for stroke that is dose- and duration- dependent, biologically plausible and interacts synergistically with other factors such as BP and risk of stroke. They are constantly generated inside cells following exposure to xenobiotics in our ambient environment [35].Heavy alcohol use likely

increases the risk of stroke by increasing the risk of hypertension, atrial fibrillation, cardiomyopathy, and diabetes [36].

Oxidative stress and stroke

Oxidative stress is an abnormal condition caused by an excess production of oxidants compared to the antioxidant, [37,38] it has been considered as the main cause of several pathologies [39], including acute ischemic stroke. Oxidative stress (OS) plays an important role in the pathogenesis of nervous tissue damage in the presence of stroke [40]. Ischaemia would be followed by reperfusion leads to increased production of free radicals (figure 1) [41]. Superoxide is one of the most important ROS in the central nervous system [CNS] [42]. Nitric oxide (NO) plays an important role in vessel dilatation and inflammation [43]. The brain is especially prone to free radical damage for several reasons. These free radicals can generate oxidative stress [44]. It is very rich in polyunsaturated fatty acids, which are particularly vulnerable to free radical induced peroxidation, but also has a low content of antioxidant enzymes, such as catalyse and glutathione peroxidase.[45].

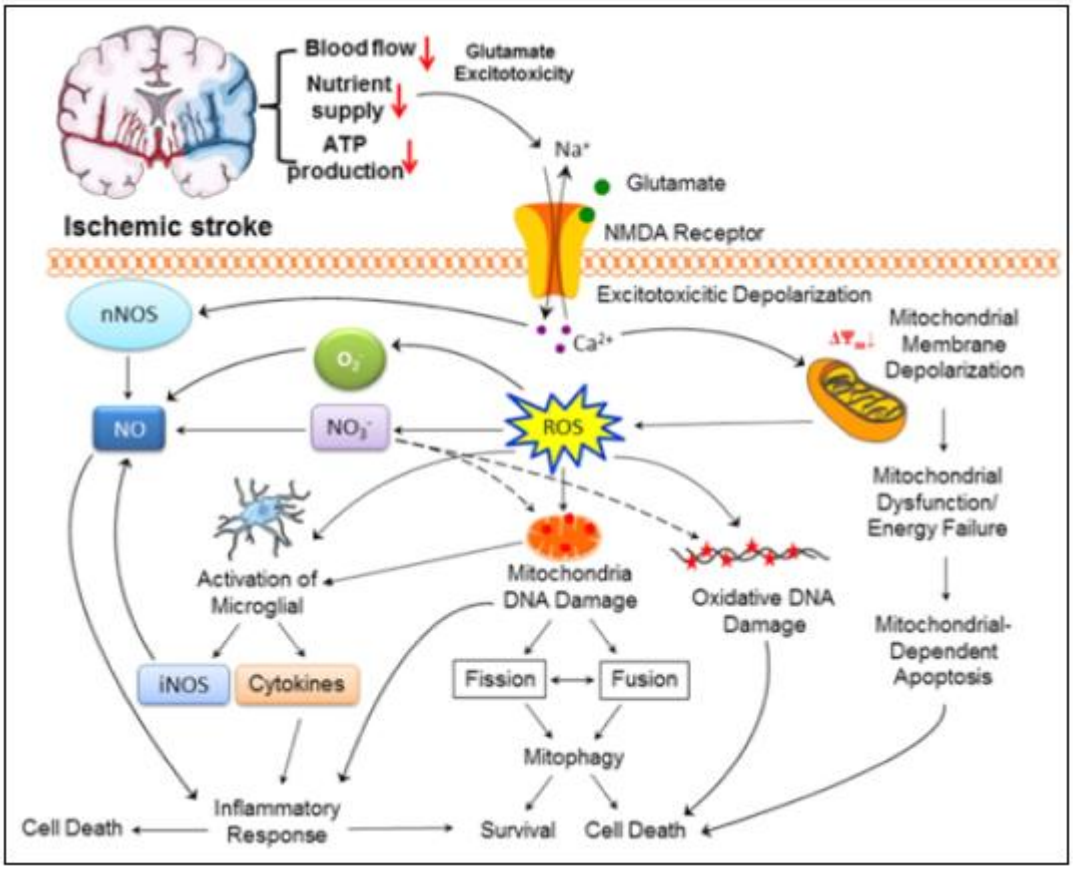

Figure 03: ROS in cerebral ischemic cascade[41]**.**

Histologically, stroke is characterized by an ischemic core [infarct] surrounded by a "penumbra" [peri-infarct] region [42], Increased production of superoxide anions, hydroxyl radicals, and peroxy-nitrite or nitrogen dioxide has been shown in infiltrating phagocytes, vascular and glial cells in the penumbra [46]. As a result, Neurons are killed rapidly within minutes and the tissue in the ischemic core is irreversibly damaged even if blood flow is reestablished [47]. Oxidativestress affect repair mechanisms and the immune control system, which is one of the main events of the inflammatory response [48]. The immune-induced inflammation. Brain ischemia and reperfusion is known to activate the complement system and form complexes such as C5b-9. Circulating dendritic cells, lymphocytes, monocytes, monocyte derived macrophages, and natural killer cells modulate inflammatory responses and thereby facilitate the thrombo-inflammatory response [49].

Conclusion

Most risk factors of stroke diseases are associated with Social behavior and lifestyle of peoples Which means that changing human behavior in life is the first way to prevent from this disease, on the other hand, stress, Oxidative stress is essential factor in the development and complication of the stoke, and therefore it is necessary to take into account the mitigation of these phenomena in any approved treatment program which contributes to the prevention or limitation of disease development.

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