INTRODUCTION

In the developed countries, stroke is the third leading cause of mortality, giving place only to cardiac and cancer diseases, as well as is the number one cause of disability in the working age population. In Russia, about 500,000 cases of acute cerebrovascular accident are reported each year; in the United States, 700,000 (of which 200,000 cases are recurrent), and in Europe, about 1.3 million. Up to 45% of patients who had stroke die in the acute phase, and the mortality rate is 50% during the first year. Among patients who survived the acute phase of stroke, about 60% have remained severely disabled and only 20% of them are able to return to work ***(Ahmedov et al., 2013).***

About 20% of strokes result from narrowing of the carotid artery, which is the main artery supplying blood to the brain. Blood clots can form at the point of narrowing. If a blood clot breaks off into the bloodstream, it can be carried into thebrain, block the blood supply there and cause a stroke. A surgical operation known as carotid endarterectomy removes the inner lining and blood clot in the carotid artery and can lower the risk of Stroke ***(Vaniyapong et al., 2013).***

Carotid endarterectomy (CEA), a prophylactic procedure used in vascular surgery,is performed in patients at risk of stroke from emboli arising from atheromatous plaque at the carotid bifurcation. The first successful carotid endarterectomy (CE) was done by Michael E. DeBakey in 1953 ***(Easton, 2014).***

The aim of CEA is to decrease subsequent risk of fatal or disabling stroke in patients with significant carotid stenosis, but the benefits are only realized if perioperative morbidity and mortality are low. Patients likely to benefit from this procedure may be divided into two groups symptomatic, those with active plaques that enter the cerebral circulation and cause transient ischemic attacks (TIAs), and asymptomatic, those with significant carotid stenosis at the bifurcation, but with no history of TIAs or strokes.

Carotid endarterectomy can be performed by diffrent anaesthetic modalities both regional and general anaesthesia. However, which anaesthetic method is superior in regard to postoperative outcomes remains controversial ***(Williams and Barroga, 2015).***

Aim of the Essay

The main purpose of this essay is to discuss anaesthetic management, different ways of anesthesia and postoperative complications of carotid endartrectomy.

ANATOMY AND PATHOPHYSIOLOGY

Anatomy overview

The aortic arch provides the great vessels, including the innominate artery, the left common carotid artery (CCA), and the subclavian artery. On each side, the CCA travels within the carotid sheath before branching into the ipsilateral internal carotid artery (ICA) and external carotid artery (ECA). The ECA primarily supplies blood to the face and includes branches of the superior thyroid and ascending pharyngeal arteries. The ICA has no extracranial branches. The ICA embryologically develops from the third primitive aortic arch. This artery arises from the CCA in the neck entering the head at skull base via the carotid canal. It terminates at the bifurcation into the anterior cerebral artery (ACA) and middle cerebral artery (MCA). This bifurcation is often referred to as the "carotid T" because of its shape or the "top-of-the carotid" because of its location. The carotid sinus is a baroreceptor located at the carotid bifurcation (where the CCA bifurcates into the ICA and the ECA) and is innervated by the nerve of Hering, a branch from cranial nerve IX (the glossopharyngeal nerve). The carotid bifurcation also contains the carotid body, which functions as a chemoreceptor responding to low oxygen levels or high carbon dioxide levels.

Pathophysiology

Acute ischemic strokes result from vascular occlusion secondary to thrombo embolic disease. Ischemia causes cell hypoxia and depletion of cellular adenosine triphosphate (ATP). Without ATP there is no longer energy to maintain ionic gradients across the cell membrane and cell depolarization. Influx of sodium and calcium ions and passive inflow of water into the cell lead to cytotoxic edema ***(Donnan et al., 2008).***

Ischemic core and penumbra

An acute vascular occlusion produces heterogeneous regions of ischemia in the affected vascular territory. Local blood flow is limited to any residual flow in the major arterial source plus the collateral supply. Any Affected regions with cerebral blood flow of lower than 10 mL/100 g of tissue/min are referred to collectively as the core. These cells are presumed to die within minutes of stroke onset. Zones of decreased or marginal perfusion (cerebral blood flow < 25 mL/100g of tissue/min) are collectively called the ischemic penumbra. Tissue in the penumbra can remain viable for several hours because of marginal tissue perfusion ***(Latchaw et al., 2003).***

Ischemic cascade

On the cellular level, the ischemic neuron becomes depolarized as ATP is depleted and membrane ion-transport systems fail. Disruption of cellular metabolism also impairs normal sodium-potassium plasma membrane pumps, producing an intracellular increase in sodium which in turns increases intracellular water content. This cellular swelling is referred to as cytotoxic edema and occurs very early in cerebral ischemia. Cerebral ischemia impairs the normal sodium-calcium exchange protein also found on cell plasma membranes. The resulting influx of calcium leads to the release of a number of neurotransmitters, including large quantities of glutamate, which in turn activates N -methyl-D-aspartate (NMDA) and other excitatory receptors on other neurons ***(Kasner and Grotta, 2003).***

These neurons then become depolarized, causing further calcium influx, further glutamate release, and local amplification of the initial ischemic insult. This massive calcium influx also activates various degradative enzymes, leading to the destruction of the cell membrane and other essential neuronal structures. Within hours to days after a stroke, specific genes are activated, leading to the formation of cytokines and other factors that, in turn, cause further inflammation and microcirculatory compromise. Ultimately, the ischemic penumbra is consumed by these progressive insults, coalescing with the infarcted core, often within hours of the onset of the stroke. Infarction results in the death of astrocytes, as well as the supporting oligodendroglial

and microglial cells. The infarcted tissue eventually undergoes liquefaction necrosis and is removed by macrophages, with the development of parenchymal volume loss. A well-circumscribed region of cerebrospinal fluid–like low density, resulting from encephalomalacia and cystic change, is eventually seen. The evolution of these chronic changes may be seen in the weeks to months following the infarction ***(Kasner and Grotta, 2003).***

Hemorrhagic transformation of ischemic stroke

Hemorrhagic transformation represents the conversion of an ischemic infarction into an area of hemorrhage. This is estimated to occur in 5% of uncomplicated ischemic strokes, in the absence of fibrinolytic treatment. Hemorrhagic transformation is not always associated with neurologic decline, with the conversion ranging from the development of small petechial hemorrhages to the formation of hematomas that produce neurologic decline and may necessitate surgical evacuation or decompressive hemicraniectomy. Proposed mechanisms for hemorrhagic transformation include reperfusion of ischemically injured tissue, either from recanalization of an occluded vessel or from collateral blood supply to the ischemic territory or disruption of the blood-brain barrier. With disruption of the blood-brain barrier, red blood cells extravasate from the weakened capillary bed, producing petechial hemorrhage or more frank intra parenchymal hematoma. Hemorrhagic transformation of an ischemic infarct occurs within 2-14 days postictus, usually within the first week. It is more commonly

seen following cardio-embolic strokes and is more likely to occur with larger infarct volume ***(Mullins et al., 2005).***

Poststroke cerebral edema and seizures

Although clinically significant cerebral edema can occur after anterior circulation ischemic stroke, it is thought to be somewhat rare (10-20%). Edema and herniation are the most common causes of early death in patients with hemispheric stroke. Seizures occur in 2-23% of patients within the first days after ischemic stroke. A fraction of patients who have experienced stroke develop chronic seizure disorders ***(Adams et al., 2007).***

Etiology

Ischemic strokes result from events that limit or stop blood flow, such as extracranial or intracranial thrombotic embolism, thrombosis in situ, or relative hypoperfusion. As blood flow decreases, neurons cease functioning. Although a range of thresholds has been described, irreversible neuronal ischemia and injury is generally thought to begin at blood flow rates of less than 18 mL/100 g of tissue/min, with cell death occurring rapidly at rates below 10 mL/100 g of tissue/min.

Risk factors

Risk factors for ischemic stroke include modifiable and nonmodifiable conditions. Identification of risk factors in each

patient can uncover clues to the cause of the stroke and the most appropriate treatment and prevention plan.

Carotid Stenosis

Atherosclerotic disease occurs frequently at the common carotid artery bifurcation. Such extracranial atherosclerotic disease accounts for 15% to 20% of ischemic strokes. Traditional imaging-based risk assessment of stroke, focused on defining the degree of arterial narrowing. When carotid stenosis is severe and reduces cerebral perfusion pressure (CPP), autoregulation of the vasculature will maximally dilate the cerebral arterioles to maintain cerebral blood flow. With further reduction in cerebral perfusion pressure and maximally dilated arterioles, the cerebral blood flow will also decrease and potentially increase the risk of stroke. CPP, is the net pressure gradient causing cerebral blood flow to the brain (brain perfusion). It must be maintained within narrow limits because too little pressure could cause brain tissue to become ischemic, and too much could raise intracranial pressure. CPP is normally between 70 and 90 mmHg in an adult human ***(Chaturvedi et al., 2005).***

The prevalence of asymptomatic carotid stenosis >50% increases with age and in patients with coronary heart disease, smoking, and diabetes mellitus. On the other hand, patients with carotid stenosis have a 4-fold higher risk of myocardial infarction than stroke ***(Goessens et al., 2007).***

While endarterectomy of symptomatic carotid stenosis is a proven and beneficial treatment for secondary stroke prevention, its value for asymptomatic stenosis remains controversial. Randomized trials from the nineties have suggested a benefit for surgery in asymptomatic carotid stenosis of ≥ 60% to ≥ 70% (relative risk reduction by 50%), provided the perioperative complication risk is less than 3% and patients have a life expectancy ≥ 5 years. Considering the absolute risk reduction of 1% per year, however, the treatment effect was rather low. Moreover, recent studies suggested a stroke risk of <1% per year for patients with asymptomatic carotid stenosis and treated with intensive medical therapy, which was primarily attributed to regular use of antihypertensive drugs and statins and lifestyle modification ***(Halliday et al., 2007).***

Arterial Hypertension

The relationship between blood pressure and stroke risk is linear and continuous as the reduction of borderline hypertension Systolic blood pressure (SBP 130–140 mm Hg and diastolic blood pressure (DBP 85–89 mm Hg) was also associated with risk reduction of stroke. Treatment of isolated SBP in elderly patients is also preventive, reduction of SBP >160 mm Hg to 145 mm Hg in patients aged >80 years was associated with stroke reduction by 30% within 2 years. Efficacious reduction of blood pressure is much more important and essential for stroke prevention than the choice of antihypertensive drugs. The selection of drug class should be

made based on comorbidities. Some studies and meta-analyses suggest a beneficial trend in favor of calcium antagonists and angiotensin-converting enzyme blockers ***(Beckett et al., 2008).***

Whereas beta blockers in hypertensive patients without heart disease seem to be less protective for stroke prevention. Recent studies indicate that a high variability in blood pressure is associated with a higher stroke risk, which again supports treatment with calcium antagonists. Indications for the use of antihypertensive drugs depend on blood pressure values and the vascular risk profile; thus, treatment should be initiated earlier in patients with diabetes mellitus or in those with a high vascular risk profile. In patients with a low risk profile and borderline blood pressure values, non-pharmaceutical treatment options should be used. Antihypertensive drug treatment is recommended for all patients with blood pressure >140/90 mm Hg, whereas the treatment goal in high-risk patients should be ideally blood pressure levels of <130/80 ***(Rothwell et al., 2010).***

Diabetes Mellitus

Patients with diabetes mellitus have a higher risk of vascular events. According to a prospective observational study, patients with type 2 diabetes suffered more frequently from stroke than from myocardial infarction ***(Martin et al., 2007).***

Diabetes promotes cerebral microangiopathy and causes lacunar type strokes. Current data indicate that metformin may

be beneficial for stroke prevention in diabetes. Intense control of hyperglycemia rather reduces microvascular complications, whereas the effect on macrovascular complications such as stroke is not clear ***(Gerstein et al., 2011).***

Moreover, intense control of present vascular risk factors such as hypertension or dyslipidemia has been shown to efficiently reduce the risk of cardiovascular events in diabetic patients. In addition, the use of statins has been shown to significantly reduce stroke risk ***(Gaede et al., 2003).***

Atrial Fibrillation

The prevalence of atrial fibrillation increases with age (1% in 60-year-old patients, 18% in patients aged >85 years). It is the leading cause of stroke in the elderly and is associated with large infarcts and high mortality rates. A regular pulse palpation in patients aged >65 years and electrocardiography in the case of arrhythmic heart rate is recommended by cardiology societies to detect atrial fibrillation and prevent ischemic stroke ***(Camm et al., 2010).***

Sleep Disordered Breathing

Sleep disordered breathing has been increasingly recognized as an independent risk factor for stroke. It can be the cause and the consequence of stroke. The high frequency (50–70%) of SDB in stroke patients, often in the form of obstructive sleep apnea (OSA), justifies the routine implementation

of screening tools such as respiratory polygraph or apnea check ***(Hermann and Bassetti, 2009).***

In severe OSA, treatment with continuous positive airway pressure (CPAP) may reduce the cardiovascular morbidity and mortality, limited ***(Barbe et al., 2012).***

Dyslipidemia and Statins

The association between stroke and hypercholesterinemia is less clear, although it is an established risk factor for myocardial infarction. Many studies indicate an increased risk of ischemic stroke with higher serum cholesterol levels (>7 mmol/l). Hypercholesterinemia is clearly related to carotid atherosclerosis. Whereas HDL-cholesterol is inversely associated with the risk of ischemic stroke. Statins have been shown to prevent stroke markedly in patients with coronary heart disease, diabetes mellitus, or carotid stenosis, whereas this was not the case for the use of fibrates. The action of statins is assumed to be mediated through multiple effects (anti-inflammatory, immunomodulatory, plaque stabilizer, vasodilatation) ***(Endres, 2005).***

Smoking

Cigarette smoking is an independent risk factor for stroke and potentiates the effect of other risk factors such as hypertension or hormone replacement therapy. The mechanism is due to reduced endogenous fibrinolysis and increased thrombocyte activity. Recent studies also suggest an association

between passive smoking and stroke. Stroke risk was reduced by 50% one year after quitting smoking, and was comparable to that of nonsmokers 5 years later ***(Wilson et al., 1997).***

Genetic and inflammatory mechanisms

Evidence continues to accumulate that inflammation and genetic factors have important roles in the development of atherosclerosis and specifically in stroke. According to the current paradigm, atherosclerosis is not a bland cholesterol storage disease, as previously thought, but a dynamic chronic inflammatory condition caused by a response to endothelial injury. Host genetic factors moreover, may modify the response to these environmental challenges, although inherited risk for stroke is likely multigenic. Even so, specific single-gene disorders with stroke as a component of the phenotype demonstrate the potency of genetics in determining stroke risk. A number of genes are known to increase susceptibility to ischemic stroke. Mutations to the *F2* and *F5* genes are relatively common in the general population and increase the risk of thrombosis. Mutations in the following genes also are known to increase the risk of stroke ***(Kubo et al., 2007).***

Hyperhomocysteinemia and homocystinuria

Hyperhomocysteinemia is implicated in the pathogenesis of ischemic stroke. The most common concern is mutations in the 5, 10-methylenetetrahydrofolate reductase (*MTHFR*) gene.

In many populations, the mutant allele frequency reaches polymorphic proportions, and the risk factor for cerebrovascular disease is related to the serum level of homocysteine. Furthermore, in persons who are compound heterozygotes for *MTHFR* mutation, if elevated homocysteine is found, it can be lowered with oral folic acid therapy.In addition, hyperhomocysteinemia can be seen in cystathione beta synthetase (CBS) deficiency, which is generally referred to as homocystinuria. This disorder is inherited in an autosomal recessive manner. Symptoms usually manifest early in life. Patients have a marfanoid habitus, ectopia lentis, and myopia and generally have intellectual disability ***(Mudd et al., 1985).***

Thromboembolic events are the most common cause of death for patients with homocystinuria and may be of any type, including myocardial infarction. The risk of having a vascular event in homocystinuria is 50% by age 30. It was previously suggested that persons who are heterozygous for mutations in the CBS gene may have an increased risk of cerebrovascular disease as well, but several more recent studies on this subject failed to replicate this finding ***(Testai and Gorelick, 2010).***

CADASIL

Cerebral arteriopathy, autosomal dominant, with subcortical infarcts and leukoencephalopathy (CADASIL), is caused by mutations in the *NOTCH3* gene. It affects the small arteries of the brain. Strokelike episodes typically occur at a mean age of