Ischaemic stroke – one of the most frequent causes of disability

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Abstract

Ischaemic stroke is one of the most frequent causes of adult disability. Even with best stroke unit care, only about one third of patients recover without any neurologic deficits. This is a great health problem, especially in modern societies.

Depending on its etiopathogenesis, ischaemic stroke can be divided into thrombotic, embolic and haemodynamic. Frequent sources of artery embolism are atheromatous plaques within cephalad arteries, followed by cardiac diseases, e.g. atrial fibrillation.

The most advanced method of treatment for acute ischaemic stroke is thrombolysis with the use of recombinant tissue plasminogen activator (rt-PA).

According to the European Stroke Initiative recommendations, each stroke patient should undergo early rehabilitation adjusted to patient's individual needs.

The central nervous system maintains regenerative capacities in post-stroke patients. These capabilities are of value throughout life, regardless of age. Therefore, it should be beneficial to start rehabilitation at any time after stroke.

The World Health Organisation defines a stroke as a clinical syndrome characterized by rapidly developing symptoms of focal and global loss of cerebral function, lasting > 24h or leading to death with no apparent cause other than that of vascular origin.

According to the American National Institute of Neurological Disorders and Stroke, a stroke is a syndrome of symptoms resulting from transient or permanent functional impairment of the central nervous system caused by the ischaemic or haemorrhagic process, in which one or many cerebral vessels have been primarily injured by the pathological process. This more precise definition clearly distinguishes ischaemic and haemorrhagic stroke, which is essential for the entire therapeutic process as the management of stroke patients depends markedly on the type of stroke. Impaired inflow of blood to the brain causes about 80% of strokes while haemorrhagic strokes occur in the remaining 20% of cases [24, 30].

Epidemiology

The incidence rate of ischaemic stroke is substantially higher in the elderly (above the age of 65-70 years). It is the third leading cause of death and the most common cause of permanent disability in this age group. The disease is slightly more common in men than in women, which equalises in the older age due to longer survival rates amongst the latter.

The annual incidence of stroke is estimated at 110-290/100 000 inhabitants in Western Europe and the United States. In Poland, this incidence is comparable yet the stroke-related mortality is found to be much higher – about 40% versus 18-25% in the West [24].

Populations of developed countries age; therefore, the incidence rates should be expected to increase in the nearest future although the risk of modifiable factors has been observed to decrease in some countries. These factors include heart diseases, particularly affecting its conduction system, such as atrial fibrillation, impaired lipid metabolism, arterial hypertension, elevated levels of fibrinogen and haematocrit, obesity, diabetes mellitus, hypothyroidism, nicotine and lack of physical activity.

The non-modifiable factors (that cannot be changed) include:

- age > 65 years, the risk of stroke doubles with each subsequent decade of life,
- gender – the incidence of stroke is slightly higher in men than in women,
- genetic factors – higher incidence rates have been observed in some families,
- race – higher incidence of stroke in Blacks compared to Caucasians [14].

Etiopathology

Ischaemic stroke is a polyetiologic phenomenon, i.e. can result from many diseases, those affect-

ting brain vessels, general diseases as well as remote pathological processes. In general, depending on the pathogenetic mechanism, ischaemic stroke can be divided into thrombotic, embolic, lacunar - predominantly caused by obstruction of small vessels, and haemodynamic, which can result from a decrease in systemic arterial pressure.

The thrombotic mechanism is usually associated with atherosclerosis and mainly regards large arterial trunks.

In many cases, emboli reach the brain through the cardiac cavities at their incomplete emptying during systole, as observed in common atrial fibrillation cases. They predominantly regard small and medium intracranial arteries. Increased incidence of atrial fibrillation is observed, most commonly tachyarrhythmia, associated with population ageing, hence increased numbers of patients with atherosclerosis and arterial hypertension [36]. Moreover, there is evidence that proneness to atrial fibrillation is conditioned genetically [52]. Cerebral artery embolism can also develop due to detachment of a thrombus from the atherosclerotically altered internal carotid and vertebral arteries [2].

Distinct symptoms of cerebral tissue ischaemia occur when the local flow decreases below 22ml/100g/min (normal values - about 50 ml/100g/min). In the ischaemic area at total arrest of blood inflow, the energy deficit develops very quickly. The brain has no stores of energy substrates and depends on the continuous inflow of oxygen and glucose. Oxygen is depleted within 10 seconds; after this period, anaerobic glycolysis develops with the breakdown inhibited at the level of lactic acid (instead of passing through the stage undergoing further transformations - pyruvic acid) whose maximum concentration is achieved in less than 3 minutes. This increases acidosis in the cerebral tissue eventually leading to its necrosis [56].

Diagnosis

In a high proportion of cases, stroke-induced brain damage is associated with the impaired function both in the somatic and intellectual sphere [34]. Neurological symptoms primarily depend on the location of cerebral tissue infarct in the hemispheres, cerebellum or brain stem. According to the ischaemia-affected cerebral area, the Oxford classification divides strokes into:

- total anterior circulation infarct (TACI)
- partial anterior circulation infarct (PACI),

- posterior circulation infarct (POCI),
- lacunar cerebral infarct (LACI).

Depending on symptoms, ischaemic conditions can be classified into:

- transient ischaemic attack (TIA), in which the symptoms subside within 24 hours,
- reversible ischaemic neurologic deficit (RIND), in which the symptoms last less than 3 weeks,
- completed ischaemic stroke (CIS), resulting in permanent neurological deficits [24].

Neurological examination

The first conclusions concerning the type of stroke, its dynamics and extent of cerebral damage can be drawn from the patient's history provided by a patient or his/her family.

Examinations start with assessment of consciousness. To put it simply, consciousness disorders can be categorised into 3 degrees:

- drowsiness with limited mental sensations - comprehension of the environment and personal experiences,
- stupor - lack of verbal contact with protective reflexes preserved,
- coma - loss of reactivity to all external stimuli.

The leading symptom of cerebral hemisphere damage with involvement of the frontal lobe is spastic hemiparesis or paresis contralateral to the injured hemisphere, which is initially flaccid. They are commonly accompanied by parietal symptoms in the form of disorders of all types of sensations, "seediness" and impaired body image awareness.

Damage to the upper motor neuron, causing the loss of motor-sensory control of muscle tone, leads to its increase in the form of spasticity. Spasticity results in a characteristic silhouette: the upper limb adducted and spastically bent in all joint, the shoulder lowered, the lower limb straight with talipes equinovarus, and heliocopod gait.

The involvement of the dominating hemisphere is associated with speech disorders: motor ones with preserved comprehension when the posterior part of the inferior frontal gyrus is damaged or sensory ones with loss of comprehension and logorrhea when the posterior part of the superior parietal gyrus is affected. Speech disorders are usually accompanied by alexia, agraphia and acalculia.

Damage to the medial cortex of occipital lobes and the tract leading to it causes contralateral hemianopsia.

When ischemia involves the cerebellar hemispheres, a triad of symptoms is observed, i.e. ataxia, nystagmus and balance disorders with falling to the hemisphere damaged. Brain stem injuries (pons and medulla oblongata) are dangerous for basic vital functions. Severe consciousness disturbances are then accompanied by impaired circulation, respiration, swallowing and expectoration [24].

The general symptoms include disturbances of higher nervous functions, i.e. emotions, perception, thinking (cognitive functions) and psychomotor drive [3].

Instrumental examinations

Modern management of stroke requires quick diagnosis. All stroke departments have to be able to provide 24-hour computed tomography (CT) and magnetic resonance imaging (MRI). During the first stage of diagnosis it is essential to determine whether a stroke is ischaemic or haemorrhagic, which usually manifests immediately as intracerebral haematoma or presence of blood in the subarachnoid spaces. Otherwise, in ischaemic stroke radiological symptoms often occur after several hours, intensify as the local oedema increases and result in necrotic lesions developing within 24-72 hours and reaching maximum clarity 3-4 days after the onset of symptoms. Therefore, when clear lesions are not observed on prompt CT, the examination should be repeated. Its spiral option enables to visualize cerebral vessels or a thrombus-induced vasoconstriction.

MRI, characterised by higher resolution, is particularly useful for detection of ischaemic lesions in the posterior cranial cavity and brain stem when bony formations hinder visualisation of lesions on CT. Additionally, MRI allows visualisation of small lesions.

Cerebral angiography with contrast medium administered to the brain-supplying arteries visualises all vascular anomalies, including constrictions or occlusions of arteries, their delaminations or various vasculopathies.

Doppler ultrasound examination also visualises lesions in the supplying and intracranial arteries but is non-invasive. It can be extremely beneficial in cases of transient ischaemic attack [20].

Patients with ischaemic stroke usually undergo a variety of necessary examinations, e.g. ECG, echocardiography, laboratory tests (cholesterol, glucose, blood clotting system).

Management in the acute post-stroke period

Treatment outcomes in patients with ischaemic stroke, mortality rates in particular, mainly depend on efficient emergency services and therapeutic teams of post-stroke departments. In the vast majority of patients, extra-cerebral causes, i.e. concomitant diseases, result in early deaths. These causes include myocardial infarction, abnormalities in conduction and rhythm, circulatory and respiratory failure, aspiration, pneumonia, decompensation of arterial hypertension, hyperglycaemia, etc.

Clinical observations have also revealed increased mortality in patients with originally elevated body temperature [45]. Moreover, early epileptic seizures worsen prognosis [5].

In the acute period, the following algorithm should be followed:

- prompt diagnosis,
- quick hospitalisation,
- intensive surveillance in life-threatening conditions,
- timely laboratory diagnostic tests,
- pharmacological therapy introduced as quickly as possible, mainly thrombolytic,
- early rehabilitation,
- early secondary prevention [24].

Depending on the severity, acute stage patients can be divided into three groups. The first one includes patients with relatively intensive neurological deficits, capable of changing the body position and with preserved contact. The second group encompasses bed-ridden patients with preserved contact. The third group patients present substantial motor deficits and consciousness disorders evidencing brain stem insufficiency. Prognosis in the first group is good, in the second group – grave and in the third one – bad in the majority of cases.

Approximately 20% of patients in the acute period require intensive surveillance, monitoring of consciousness, arterial pressure, respiration (intubation, if needed), partial pressure of O₂ and CO₂. Unconscious patients should be placed in the lateral position and frequently turned to prevent bedsores [14]. Head elevation by about 30° is to prevent deterioration of brain oedema, which can be supported by moderate hyperventilation.

Great caution should be exercised while reducing elevated arterial pressure, which can be a protective reaction compensating insufficient brain blood supply. Vigorous antihypertensive measures are needed when systolic pressure exceeds 220 mmHg and diastolic pressure is higher than 140mmHg [51].

Pharmacological treatment

For many years, acetylsalicylic acid (aspirin) of antiaggregative action has been the only and quite efficient weapon to treat and prevent ischaemic stroke recurrences. Recent studies demonstrate that the most effective drug used in the acute stage is recombinant tissue plasminogen activator (rt-PA, alteplase) [49]. Although its thrombolytic properties have been known in the United States since 1996, in Poland, rt-PA was approved in November 2003. However, its use is stipulated with rigorist rules, i.e. intravenous administration should be completed within 3 hours since the development of first stroke symptoms and it cannot be given to patients > 80 years of age [23,51].

Moreover, anticoagulants can be applied, e.g. heparin and its safer derivatives – flaxiparine and calciparine characterised by lower risk of cerebral infarct focus haemorrhaging. Attempts to introduce neuroprotective drugs have failed to confirm their efficacy [24].

Furthermore, biochemical markers, such as C-reactive proteins (CRPs), D-dimers, gamma-aminobutyric acid (GABA), neuron-specific enolase, can be of assistance for prognosis in the early post-stroke period [42].

Interventional treatment

Internal carotid and vertebral arteries constricted in 70-90% of diameter detected on vascular imaging (US-Doppler, angiography) are an indication for endarterectomy, i.e. removal of an atheromatous plaque by incising the artery, which is associated with lower number of complications, compared to angiography with stenting, particularly in patients > 70 years of age [51].

In cases of extremely increased intra-cranial pressure due to growing brain oedema and pharmacological measures fail, decompressive hemicraniectomy with duraplasty is suggested. The procedure should be considered life saving and can be recommended, especially for younger patients [44].

A common problem concerning management of patients with hemiparesis is spasticity, which in untreated cases leads to contractures substantially reducing the quality of life. Beside physiotherapeutic procedures, local injections of botulinum neurotoxin have been found beneficial [32,50].

Prophylactic management

Prophylaxis can be useful in individuals without the history of stroke but with increased risk factors, i.e. primary prophylaxis, and in post-stroke patients, i.e. secondary prophylaxis.

Primary prophylaxis

The management involves the detection of the highest possible number of risk factors and attempts to normalize them. Co-existence of abdominal obesity, arterial hypertension, increased glucose levels and disorders of lipid metabolism was named metabolic syndrome, or more emphatically “a fatal quartet” as it was recognized in half of patients with ischaemic stroke [39, 43].

In cases of abdominal obesity, weight loss is essential; a reduction by 10 kg decreases the level of cholesterol (LDL fraction) by 7% and increases the HDL fraction by 13 % [37]. Hypercholesterolemia is an indication for static drugs, particularly at the adverse LDL/HDL fraction proportion to the detriment of the latter.

A decrease in elevated arterial pressure, systolic by 10 mmHg and diastolic by 5 mmHg, reduces the risk of stroke by 40%. Pharmacological treatment involves thiazide and beta-adrenolytic drugs. It is recommended to lower the intake of table salt and its replacement with potassium and magnesium salt [18].

Moreover, it is crucial to control blood levels of glucose; when diabetes mellitus is diagnosed, it should be meticulously treated.

Atrial fibrillation increases the risk of stroke five times [1]; paroxysmal atrial fibrillation requires intensive cardiologic treatment whereas persistent atrial fibrillation should be treated with acetylsalicylic acid (or Xarelto), which prevents intracardiac thrombi.

The occurrence of transient ischaemic attack (TIA) should be a signal for vigorous diagnosis or therapeutic management as completed stroke develops after TIA in 7-14.5% of patients during the first month and even within several first days, the risk of stroke is eight-fold higher [51]. Diagnosis of such patients requires at least short hospitalization.

The cheapest and quite effective recommendation in primary prevention is to give up smoking. A clear reduction in stroke risk is achieved already 2 years after quitting smoking [24].

One of the most effective measures to prevent ischaemic stroke is high physical activity; at least 30 minutes of physical activity daily (e.g. fast walk) are recommended. The study findings have demonstrated that the risk of stroke is lower by 25 % in physically active individuals, as compared to the general population [27].

Secondary prophylaxis

After stroke, all recommendations of primary prophylaxis have to be applied. Anti-aggregative drugs are essential. The most widely used and economic drug is acetylsalicylic acid (ASA) in a most commonly recommended daily dose of 75 – 150 mg. Studies have shown that ASA reduces the risk of stroke by 15-20% after the TIA episode and mortality by 16% after completed ischaemic attack (CIA). An adverse side effect of the drug is bleeding from the digestive tract requiring protective treatment.

In high-risk patients and lack of positive reaction to ASA, thienopyridines, such as clopidogrel, in a daily dose of 75 mg, are used. However, when this treatment is applied, blood morphotic composition has to be frequently controlled, as leucopenia is likely to develop, which is a severe complication resulting in inflammatory conditions.

Post-stroke rehabilitation

The opinion that in cases of sudden onset of symptoms patients should „rest” and stay in bed for at least several days still lingers amongst older generation neurologists. It could have been justifiable when neurological diagnostic procedures to differentiate ischaemic and haemorrhagic stroke were mainly based on symptoms and the course of disease.

As the previous sections reveal, post-stroke departments have to be able to diagnose the type of stroke or at least to exclude its haemorrhagic nature immediately after admission. Therefore, rehabilitation in cases of ischaemic stroke should be initiated as soon as possible, within 48 hours after the onset at most [14]. A substantial proportion of stroke patients require such management. Even with the best treatment, including thrombolysis, less than 1/3 patients recover completely without neurological deficits [27, 40].

International organizations accepted the principles and recommendations for the treatment of stroke patients. The European section of WHO contained those guidelines in the Helsingborg Declaration (1995, 2006). The European Stroke Organization recommends that all patients in the acute post-stroke period have an access to specialist care and experienced rehabilitation teams [8]. In Poland, guidelines of the group of experts of the National Programme on Prevention and Treatment of Cardiovascular Diseases are available (POLKARD 2006) [12].

The above guidelines significantly intensified the development of post-stroke care in Poland, which is considered substantially delayed; in the 90-ties of the previous century, early rehabilitation was available to 1% of post-stroke patients [11]. Questionnaire studies have disclosed that in 2008 comprehensive early rehabilitation was conducted in 19 post-stroke departments and 38.5% of the minimum rehabilitation beds required for stroke patients were available [40]; further improvement is observed.

The integrated system of post-stroke care includes care and rehabilitation in the acute and subacute period, early in-hospital rehabilitation, post-discharge services, home care and social support [15]. To fulfil standard requirements of modern post-stroke rehabilitation, interdisciplinary teams are essential rehabilitation, consisting of a neurologist, rehabilitation specialist, physiotherapist, speech therapist, neuropsychologist, occupational therapist, social worker, and a nurse acquainted with rehabilitation issues [4].

The neurologist manages the therapeutic team, recognises neurological disorders in patients, determines real rehabilitation aims, provides medical care, particularly in prevention and treatment of complications resulting from disability or immobility.

The physiotherapist aims at maximum improvement, physical efficiency, unaided mobility, and a reduction of increased muscle tone using kinesitherapy, physiotherapies and massage. Exercises are performed with patients' active participation, if possible or passively in unconscious or severely ill patients.

The speech therapist diagnoses and rehabilitates speech disorders, especially motor aphasia, and provides instructions for patients with dysphagia.

The neurologist detects cognitive and emotional disorders, stimulates and controls improvements in these functions. Cognitive disorders are

improved using exercises regarding speech, writing, Reading, calculations, attention, perception, memory, spatial and constructive abilities, as well as performance.

The occupational therapist teaches everyday independence - dressing up, toilet, preparation of meals, eating, taking drugs, etc.

The rehabilitation team nurse is to provide routine nursing care, stimulate applications of the abilities learnt, and assist in cases of impaired functions of sphincters, whenever necessary.

The social worker takes care of social and living standards of patients.

In the chronic stage of disease, social support is essential for restoration of normal functioning. Generally, social support is defined as some auxiliary behaviour towards individuals in difficult situations [17, 28, 47, 55].

Summary and conclusions

Ischaemic cerebral stroke is the most common cause of disability in the elderly. The societies in developed countries age which can induce increasing health-related, social and economic problems.

Depending on its etiopathogenesis, strokes are divided into thrombotic, predominantly caused by atherosclerosis of brain arteries, embolic, in which thrombi most commonly come from cardiac cavities and haemodynamic induced by reduced systemic arterial pressure.

According to ischaemic conditions, strokes are classified into transient ischaemic attack, reversible ischaemic neurological deficit and completed ischaemic stroke, which leads to permanent neurological deficits.

Stroke-induced symptoms depend on the location and extent of ischaemic focus in the cerebral hemispheres, cerebellum or brain stem. The most common symptom is spastic hemiparesis with ipsilateral sensory disorders.

Instrumental examinations used include computed tomography, magnetic resonance imaging, ultrasound of cephalad arteries and cerebral angiography with contrast.

As far as the treatment is concerned, thrombolytic therapy is essential, whose use depends on quick hospitalisation of patients. In chronic stages, acetylsalicylic acid and anticoagulants are applied.

Prevention of ischaemic strokes involves elimination of basic risk factors, such as obesity, arterial hypertension, disorders of lipid metabolism, and diabetes mellitus. Moreover, physical activity is important.

Rehabilitation management depends on the severity of condition and stroke stage. In severe conditions, it is necessary to prevent complications, such as inflammatory conditions of the lungs associated with retention of secretions in the airway, urinary inflammations connected with long-term catheterisation, and sores caused by motionless, recumbent positions. Rehabilitation during further stage of stroke depends on the degree of improvement; it should be initiated as soon as possible and individually adjusted to physical and mental capacities of patients.

Best rehabilitation outcomes are achieved when patients are provided with comprehensive rehabilitation by a multi-disciplinary professional team, consisting of a neurologist, physiotherapist, neuropsychologist, rehabilitation nurse, occupational therapist, and social worker.

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