

and Nel proposed a mechanism based on brain single-photon emission computed tomography studies. These scans, performed on «zolpidem responders», showed that after zolpidem administration, there was a marked increase in blood flow to areas of the brain adjacent to or distant from the damaged tissues, such as in the contralesional (ipsilateral) cerebral hemisphere or cerebellum. These areas are believed to be inhibited by the site of injury by a GABA-mediated mechanism, and this inhibition is modified by zolpidem. Further proof of this is offered by the fact that the zolpidem effect can be blocked by flumazenil, which blocks omega-1 receptors. The idea that functional neurologic deficits are not caused solely by brain tissue death is not new and is the basis of newer rehabilitation techniques, such as constraint-induced movement therapy. Thus, this explanation for zolpidem's action is plausible and consistent with current concepts on brain plasticity, which involves cortical reorganization and activation of previous unused or underutilized pathways. Ipsilateral motor cortex areas are believed to play a role in neurologic recovery, particularly early on, and may show an inhibitory effect on the ipsilesional (contralateral) cortex via interhemispheric inhibition. This inhibition decreases with neurologic recovery. In essence, zolpidem appears to temporarily “short circuit” the recovery and learning process, which is usually required for plasticity-related neurologic recovery. That zolpidem induces sleep in normal persons but causes arousal in brain-injured patients is a remarkable paradox. Furthermore, it is not clear why the selective action of zolpidem on the omega-1 receptor acts favorably on this inhibition in brain injury, whereas classic benzodiazepines do not. Short-interval intracortical inhibition is a GABA-mediated motor cortex inhibition that is increased by benzodiazepines but not by zolpidem. Thus, the inhibition exerted by the omega-1 units, in the absence of stimulation of the other 2 subtypes, may be related to the unexpected arousal. Some patients do not respond to zolpidem; presumably, in these cases, the neurologic deficits are caused mainly by severely damaged or dead tissue rather than from inhibitory effects.

Conclusion

Given the poor prognosis of patients with chronic acquired brain injury with disorders of consciousness, zolpidem may offer great hope for patients and their families. Clearly, more work needs to be done, both to delineate the mechanisms by which this drug works and to perform controlled trials to prove effectiveness, both short- and long-term.

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INTRACEREBRAL HEMORRHAGE NON-TRAUMATIC CAUSES AND MANAGEMENT

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Introduction

The American Heart Association/American Stroke Association has defined the term intracerebral hemorrhage (ICH) as «A focal collection of blood within the brain parenchyma or ventricular system that is caused by traumatic/other metabolic causes or non-traumatic» and also causes a life-threatening type of stroke called hemorrhagic stroke (HS).

Aim

To study the clinical picture and the manifestations of intracerebral hemorrhage non-traumatic causes according to literary sources.

Materials and methods

A theoretical analysis of literary sources and a synthesis of scientific literature for 2015–2018 was used.

Results

Globally, the proportion of strokes caused by ICH varies from 9 % (Dijon, France) to 27 % (Tbilisi, Georgia), and might be as high as 33 % in Chinese populations (pooled proportion of five community-based studies). The age-adjusted HS incidence has remained unchanged in the world between 1990 and 2013. The last two decades, the HS incidence has decreased in high income countries with 19 % while it has increased by 22 % in low and middle-income countries. The over-all crude annual ICH incidence has been estimated to 24.4 per 100,000 persons (95 % CI 19.7–30.7) in pooled estimate from a meta-analysis, and has remained unchanged between 1980 and 2008. Three western European studies report a decline in ICH incidence among younger persons (< 75 years) but stable or increasing incidence among those older than 75 years. A recent Italian population-based study showed a decline in incidence in all age groups between 1994–1998 and 2011–2012. The decreased incidence in younger persons has been attributed to a decrease in hypertension related ICH while the incidence in older patients has been connected to an increased amount of lobar ICH and, possibly, to an increased use of antithrombotic medications.

Causes of ICH. Acute or chronic hypertension: Intracerebral hemorrhage causes ~10 % of strokes, and hypertension is the most common underlying cause of Non-traumatic intracerebral hemorrhage. The incidence is lower in whites than in other groups, which relates to rates of hypertension. The role of acute elevation of blood pressure in intracerebral hemorrhage is uncertain. Chronic hypertension promotes changes in the walls of penetrating small cerebral arteries and arterioles. These consist of lipohyalinosis (collagenous thickening and inflammation of the vessel wall) and fibrinoid necrosis (vessel-wall destruction with perivascular inflammation), which are associated with ischemic stroke and may also lead to the development of military (Charcot-Bouchard) aneurysms which predispose to hemorrhage.

Cerebral Amyloid Angiopathy (CAA). Cerebral amyloid (conophilic) angiopathy is characterized by β -amyloid deposits in the walls of leptomeningeal and cortical capillaries, arterioles, and small arteries. The disorder is most common in elderly patients and typically produces lobar hemorrhage at multiple sites. Risk factors include apolipoprotein E ϵ 4 and ϵ 2 alleles, anticoagulation or antiplatelet therapy, head trauma, and hypertension. Rare hereditary cases (eg, amyloid β A4 precursor protein mutations) are inherited in autosomal dominant fashion.

Pathophysiology: ICH was once considered to be a simple, monophasic, rapid bleeding event that stopped quickly as a result of clotting and tamponade. But ICH has now been shown by serial CT scans to be a dynamic and complex process involving several distinct phases. The two most important new concepts are: -that firstly, many hemorrhages continue to grow and expand over several hours after the onset of symptoms. **Expansion of hematoma:** Most hematomas result from rupture of an artery or arteriole. Their expansion is most likely due to continued bleeding from the primary source and to the mechanical disruption of surrounding vessels. Acute hypertension, a local coagulation deficit, or both may be associated with expansion of the hematoma; Secondly, most of the brain injury and swelling that occurs after ICH is the result of inflammation caused by thrombin and other end products of coagulation. **Secondary brain injury and oedema:** The hematoma initiates oedema and neuronal damage. Oedema typically develops over the first 24–96 hours and slowly resolves over several weeks. The early oedema is usually secondary to plasma proteins present in the hematoma. Subsequent clotting and complement cascade activation results in disruption of the blood-brain barrier, direct cytotoxicity and more oedema. Lysis of red blood cells with haemoglobin toxicity and formation of free radicals probably accounts for the late onset oedema, which persists for several weeks after the initial haemorrhage. Neuronal death in the region

around the haematoma is predominantly necrotic, with recent evidence suggesting the presence of programmed cell death (apoptosis). Unlike primary tissue injury from the haematoma formation, secondary brain injury and oedema are potential therapeutic targets.

Clinical features: Mainly for non-traumatic ICH(depends on its locations).

Lobar hemorrhage:

Frontal lobe: Aliabu, Contralateral hemiparesis, Bifrontal headache mild gaze preference away from hemiparesis.

Parietal lobe: Contralateral hemisensory loss, Neglect of the contralateral visual field, Headache, Mild hemiparesis and Occasionally, hemianopia.

Temporal lobe: Wernicke's aphasia, Conduction or global aphasia, Variable degrees of visual field deficit, Headache around or anterior to ipsilateral ear and agitated delirium.

Occipital lobe: Contralateral homonymous hemianopia and Ipsilateral orbital pain.

Putaminal hemorrhage. The putamen is the most common site of hypertensive ICH: Hemiparesis or hemiplegia and, to a lesser degree, hemisensory deficit; Transient global aphasia with dominant hemispheric lesions; Agnosia or unilateral neglect with non-dominant hemispheric lesions and Homonymous hemi-anopia; Contralateral gaze palsy: the patient looks toward the hematoma and away from the hemiplegia; Alloesthesia: a noxious stimulus on the side of the hemisensory disturbance is perceived at the corresponding area of the other (normal) side.

Thalamic hemorrhage. Hemisensory deficit and, to a lesser degree, hemiparesis; Anomic aphasia with impaired comprehension, with lesions of the dominant thalamus; Convergence retraction nystagmoid movements, impairment of vertical gaze and pupillary near light dissociation; Downward – inward deviation of the eyes; Unilateral or bilateral pseudo-sixth nerve paresis and Skew deviation; Conjugate gaze palsy to the side of the lesion (wrong side) or conjugate horizontal gaze deviation

Cerebellar hemorrhage. Most common in the area of the dentate nucleus: Variable degrees of alertness, Small reactive pupils, Skew deviation and Ipsilateral gaze palsy; Ocular bobbing and nystagmus toward the gaze; paresis; Ipsilateral peripheral facial weakness and Ipsilateral absence or decrease of corneal reflex; Slurred speech, Gait or truncal ataxia; Bilateral hyperreflexia and Babinski sign; Sudden occipital headache, Nausea and repeated vomiting, Dizziness, vertigo and Inability to stand.

Pontine hemorrhage. Sudden-onset coma and Quadriplegia, quadriplegia; Respiratory abnormalities; Hyperthermia, Pinpoint reactive pupils; Eyes fixed in a central position, Loss of brain stem reflexes, including the oculocephalic (doll's head) & oculo-vestibular reflexes and Ocular bobbing. Headache, vomiting, vertigo, dysarthria, Sudden loss of consciousness, often progressing into deep coma.

Modifiable risk factor: Hypertension, Current smoking, Excessive alcohol consumption, Decreased LDP, low triglycerides, Uses of anti-platelet agent, Sympathomimetic drugs.

Non-modifiable risk factor: old age, Male sex, Asian ethnicity, Cerebral amyloid angiopathy, Cerebral microbleeds, Chronic kidney diseases.

Management for ICH:

Initial medical care: Manage clinical seizures with appropriate antiepileptic therapy. Prophylactic anticonvulsant medication should not be used. Normotonic fluids are strongly recommended. Avoid hypotonic fluids to prevent exacerbating brain edema. Treat sources of fever and administer acetaminophen to lower temperature in febrile patients. Treat hypoglycemia / hyperglycemia. Arterial line placement for continuous BP monitoring. Continuous EEG: Depressed clinical exam inconsistent with the neurological deficits of ICH.

Surgical care: Ventricular drainage as treatment for hydrocephalus is reasonable in patients with decreased level of consciousness. For patients with cerebellar hemorrhage > 3 cm, who are deteriorating neurologically or who have brain stem compression and/or hydrocephalus

from ventricular obstruction, surgical removal of the hemorrhage should occur as soon as possible. Consider injection of alteplase (TPA) into hematoma, minimally invasive clot evacuation, decompressive craniectomy, or evacuation of supratentorial ICH by standard craniotomy for select patients. The patient should be assessed by the neurosurgeon both before and after surgery.

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LAMBERT-EATON MYASTHENIC SYNDROME

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Introduction

Lambert-Eaton myasthenic syndrome (LEMS) is a rare autoimmune disease producing antibodies against pre-synaptic voltage-gated calcium channels. It can occur sporadically or as a paraneoplastic syndrome, most often associated with small cell carcinoma of the lung. The clinical presentation may be mistaken for myasthenia gravis, as there are some similarities in their pathophysiology. Lambert and colleagues first described weakness due to neuromuscular transmission deficiency in association with malignancy in the 1950s. In the 1970s, an autoimmune etiology was suggested in LEMS seen in association with other autoimmune disorders. The autoimmune theory was confirmed in the early 1980s by a series of studies resulting in normal rats developing LEMS after injecting them with immunoglobulin G (IgG) antibodies from diseased rats.⁴ Antibody blockage of the P/Q voltage-gated calcium channels was identified in the 1990s as the major etiology of the disease process of LEMS.

Aim

To study the clinical picture and the manifestations of Lambert-Eaton syndrome according to literary sources.

Materials and methods

A theoretical analysis of literary sources and a synthesis of scientific literature for 2015–2018 was used.

Results

Clinical Presentation. LEMS usually presents in adulthood, usually over 40 years of age, although it can present at any age. Due to similarities in clinical presentation, LEMS can be easily mistaken for myasthenia gravis (MG). Wirtz and colleagues examined the patterns of weakness between MG and LEMS and found that MG involved ocular muscles and bulbar muscles more prominently than LEMS. In addition, all LEMS patients in their study had lower extremity involvement, although the lower extremities were spared in a significant proportion of MG patients.

Proximal muscle weakness, greater in the lower extremities than in the upper extremities, is the typical clinical presentation. The weakness is exacerbated by exercise and heat. Rarely, cranial nerve symptoms such as ptosis, difficulty swallowing, and double vision may also be present. However, if ocular weakness is the only finding, then another diagnosis should be considered. Respiratory failure is rarely the presenting symptom in LEMS patients, although it can develop later in the disease process. Autonomic dysfunction, including dry mouth, blurred vision, constipation, and orthostatic hypotension, occurs in up to 75 % of patients. To direct muscle strength testing, the patient may seem minimally weak. This is due to the nearly continuous influx of calcium and its buildup in the presynaptic nerve terminal with exercise.