

Cerebroprotein hydrolysate: Innovation in Neurodegenerative disorders

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ABSTRACT

Stroke, traumatic brain injury and neurodegenerative disorders are one of the leading causes of death and disability in both developing and developed countries. A number of drugs including neurotrophic drugs are available for these disorders. Cerebroprotein hydrolysate is the latest one offering new hopes to patients suffering from these disorders. Its superiority is because of different actions which help in faster and more complete nerve repair and growth than other neurotrophic agents. It acts by multiple mechanisms viz.-regulation and improvement of the neuronal metabolism, modulation of the synaptic plasticity, promoting neuronal differentiation and protection against ischemic and neurotoxin lesion, reducing excitotoxic damage, blocking over activation of calcium dependent proteases, and scavenging free oxygen radicals. Till now no serious adversity has been reported.

Keywords: Neurodegenerative disorders, cerebroprotein hydrolysate, neurotrophic factors, calpain

Epidemiologic Considerations

Ischemic stroke, traumatic brain injury, vascular dementia and Alzheimer's disease collectively are responsible for major part of morbidity and mortality in geriatric as well as young adult population. Stroke ranks as the third leading cause of death in the United States. It is estimated that there are more than 700 000 incidents of strokes happening annually and 4.4 million stroke survivors. ^[1] In USA on an average, approximately 1.7 million people sustain a traumatic brain injury annually. ^[2]

In a study it is found that on an average, in the USA, 1300/100,000 people suffer concussions each year. ^[3] Out of

those who receive treatment 25 patients die. Neurodegenerative diseases that affect the affective, cognitive and psychomotor functions in the elderly compromise the quality of life of more than 24 million people across the world. ^[4] These disorders pose some of modern medicine's most difficult challenges. Common pathophysiologic feature in all of these conditions is same i.e. functional loss of neurons.

Pathophysiology of neuron

Neuron is the basic structural and functional unit of nervous system. Although there are some variations depending on the

type of neurons; they all contain four parts: cell body, dendrites, axon and axon terminal. They develop from the neural stem cells known as type 1 cells which produce progeny called amplifying neural progenitor cells (also known as type 2 cells) which proliferate and differentiate into mature neurons. Till recent past it was believed that there is no way to repair a damaged neuron. One of the main goals of researchers involved in treatment of neurodegenerative disorders is to develop drugs to stimulate nerve repair itself. [5] Several drugs like Edaravone, Citicoline and Piracetam have been developed based on neurotrophic factors. Neurotrophic factors are small proteins that exert survival-promoting and trophic actions on neuronal cells. [6] These neurotrophic factors are NGF (Nerve growth factor), BDNF (Brain-derived neurotrophic factor), NT-3 (Neurotrophin-3), GDNF (Glial cell-derived neurotrophic factor), GAP-43 (growth associated protein 43) and CNFT (Ciliary neurotrophic factor).

Glial cells continue to undergo cell division in adulthood and their ability to proliferate is particularly noticeable after brain injury (e.g stroke). [7] This is not the case with neurons; they cannot divide themselves but they undergo a lot of activity after injury. Interestingly, studies demonstrate that neurons in the adult brain have an unappreciated capacity for remodeling away from the actual injury, and that these neurons are attempting to rewire the brain following an injury. [8]

Cerebroprotein hydrolysate is the latest weapon in the physician's armamentarium. It is a neurotrophic drug. It consists of short biological peptides which act like endogenous neurotrophic factors.

Pharmacokinetics

It is given in a dose of 60 -180 mg once daily for 10-20 days. It should be slowly infused in 250 ml saline in 60-120 minutes. Maintenance doses (30 mg) can be given by i.m route. It should not be mixed with amino acid solutions in the infusion bottle. Doses of antidepressants should be reduced if used with Cerebroprotein hydrolysate.

Adverse effects and Contraindications

Studies [9, 10] have revealed that most of the side effects are minor. Most common side effects include headache, nausea, vertigo, increased sweating, agitation, fever, hallucinations, confusion, and flu like syndrome. Contraindications include hypersensitivity, epilepsy and severe renal impairment. Safety has not been established in pregnancy and lactation.

Indications

- Acute ischemic stroke
- Traumatic brain injury
- Vascular dementia
- Alzheimer's disease

Mechanism of action and pharmacological effects

It acts by multiple mechanisms viz.—

- Regulation and improvement of the neuronal metabolism.
 - Modulation of the synaptic plasticity.
 - Neuronal differentiation and protection against ischemic and neurotoxin lesion.
 - Cerebroprotein hydrolysate reduces excitotoxic damage, blocks over activation of calcium dependent proteases, and scavenges free oxygen radicals.
- Cerebroprotein hydrolysate has been shown to counteract the negative effect of

the elevated EGF-2 on neurogenesis and neuromodulation.^[11]

Cerebroprotein hydrolysate - augmented proliferation, differentiation, and migration of adult sub ventricular zone (SVZ) neural progenitor cells results in increased number of neural progenitor cells and neuroblasts to contribute to neurogenesis. This may be the mechanism for beneficial effect in acute ischemic stroke and traumatic brain injury.

Enhancement of neuronal survival is produced through effect on calpain. The hyper activation of calpain is implicated in a number of neurodegenerative disorders. Calpain is inhibited by Cerebroprotein hydrolysate

Neuromodulatory effect is produced by increasing glucose transporter1 (GLUT-1) expression which is responsible for more than 90% of glucose transport to brain.^[12]

Neuronal plasticity is produced by reduction of amyloid beta accumulation, increased MAP 2 and Synaptophysin synthesis.

Neuro-immunotrophic activity is produced by inhibition of microglial activation and expression of IL-1 beta. This results in reduction of inflammation. Other neurotrophic drugs and nootropics are not having so much broad spectrum of different actions possessed by Cerebroprotein hydrolysate. The patients of neurodegenerative disorders now can be managed in a better way with the advent of Cerebroprotein hydrolysate

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