Cerebroprotein hydrolysate: Innovation in the treatment of neurodegenerative disorders
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Abstract
Neurodegenerative disorders are one of the leading causes of death and disability in both developing and developed countries. There are a number of neurotrophic drugs used in these disorders. Cerebroprotein hydrolysate is the latest one launched in more than 40 countries. Its superiority is because of different actions which help in faster and more complete nerve repair and growth than other neurotrophic agents. Different mechanisms include regulation and improvement of the neuronal metabolism, modulation of the synaptic plasticity, neuronal differentiation and protection against ischaemic and neurotoxic lesions, cerebroprotein hydrolysate reduces excitotoxic damage, blocks over-activation of calcium dependent proteases, and scavenges free oxygen radicals.

Epidemiology
Ischaemic stroke, traumatic brain injury, vascular dementia and Alzheimer’s disease (AD) collectively are responsible for a 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 now estimated that there are more than 700,000 incident strokes annually and 4.4 million stroke survivors\(^1\). In the USA on an average, approximately 1.7 million people sustain a traumatic brain injury annually\(^2\).

Roughly speaking, in the USA alone, 1,300/100,000 people suffer concussions each year. Of these, 300/100,000 are treated in emergency departments. Of these, 90/100,000 are retained in the hospital. Around 25/100,000 die\(^3\). AD and other degenerative diseases that affect the cognitive functions in the elderly compromise the quality of life for more than 24 million people across the world\(^4\).

Besides the above-mentioned illnesses, other neurodegenerative disorders like amyotrophic lateral sclerosis, Friedreich’s ataxia, Huntington’s disease, Parkinson’s disease, and Lewy-body disease pose some of modern medicine’s most difficult challenges. The common pathophysiologic feature in all these conditions is the same, i.e., functional loss of neurons.

Development, basic structure, and repair of neurons
Neuron is the basic structural and functional unit of the 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 is to develop drugs to stimulate areas of the brain to repair itself by replacing its own cells\(^1\). Several drugs like edaravone, citicoline, and piracetam have been developed based on these neurotrophic factors. Neurotrophic factors are small proteins that exert survival-promoting and trophic (derived from the Greek meaning “to nourish”) actions on neuronal (or nerve) 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, but they undergo a lot of activity after injury. Treatment of these neurodegenerative disorders is changing at a remarkable pace. Interestingly, studies demonstrate that neurons in the adult brain have an unappreciated capacity for remodelling away from the actual injury, and that these neurons are attempting to re-wire 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. Neurotrophic activity can be detected up to 24 hours after a single injection.

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has been approved in a number of European and Asian countries.

**Pharmacokinetics**

It is given in a dose of 60 -180 mg once daily for 10 - 20 days. It should be slowly perfused in 250 ml saline in 60 - 120 minutes. Maintenance doses (30 mg) can be given by intramuscular route. It should not be mixed with balanced aminoacid solutions in an infusion. Dose of antidepressants should be reduced if used with cerebroprotein hydrolysate.

**Adverse effects and contraindications**

Studies9,10 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; so should be used cautiously in humans.

**Indications**

a) Acute ischaemic stroke.
b) Traumatic brain injury.
c) Vascular dementia.
d) Alzheimer’s disease (AD).

**Mechanism of action and pharmacological effects**

Cerebroprotein hydrolysate acts by:-

a) Regulation and improvement of the neuronal metabolism.
b) Modulation of the synaptic plasticity.
c) Neuronal differentiation and protection against ischaemic and neurotoxic lesions.
d) 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 FGF-2 on neurogenesis and neuromodulation11. This could be the mechanism for its beneficial effect in Alzheimer’s disease.

Cerebroprotein hydrolysate-augmented proliferation, differentiation, and migration of adult SVZ neural progenitor cells results in increased number of neural progenitor cells and neuroblasts to contribute to neurogenesis. This may be the mechanism for its beneficial effect in acute ischaemic 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 GLUT-1 expression which is responsible for more than 90% of glucose transport to brain11.

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.

This drug can be given with other neuroprotective agents like edaravone, citicoline, and piracetam safely. Other neurotrophic drugs and nootropics are not having as much broad spectrum of different actions as possessed by cerebroprotein hydrolysate. The patients of neurodegenerative disorders can now be managed in a better way with the advent of cerebroprotein hydrolysate.

**References**