
INTEGRATIVE AND ALTERNATIVE TREATMENTS FOR NEURODEGENERATIVE DISEASES

DR. SWAROOPA. MARALLA, D. BHARATHI

Abstract: The etiopathology of neurodegenerative diseases is extremely complex and yet has not been fully revealed. Acute and chronic neurodegenerative diseases, including prion disease, frontotemporal dementia, Pick's disease, progressive supranuclear palsy, spinocerebellar ataxias, brain trauma, amyotrophic lateral sclerosis (ALS), Huntington's disease, Alzheimer's disease, and Parkinson's disease (PD), are illnesses associated with high morbidity and mortality rates. Multiple biological processes such as depletion or insufficient synthesis of neurotransmitters, oxidative stress and abnormal ubiquitination are linked to neurodegenerative diseases. Based on the limited knowledge available about the pathogenic mechanisms of these diseases, many synthetic drugs have been developed and are currently being used but not without side effects which sometimes are more a menace than the disease itself. There are no effective treatments that can cure neurodegenerative diseases in modern society. Currently researchers aim at improving the activities of daily living in patients with degenerative disease by complementary and alternative medicine or integrative medicines and have also focused on increasing the ability of reserve to protect the mobility of degenerative disease patients by integrative medicine.

Keywords: Neurodegenerative Diseases, Biological Processes, Pathogenic Mechanisms, Complementary and Alternative Medicine, Integrative Medicine.

Introduction : Neurodegenerative diseases are characterized by protein aggregates and inflammation as well as oxidative stress in the central nervous system (CNS). Multiple biological processes are linked to neurodegenerative diseases such as depletion or insufficient synthesis of neurotransmitters, oxidative stress, abnormal ubiquitination. Furthermore, damaging of blood brain barrier (BBB) in the CNS also leads to various CNS-related diseases.

According to University of California, San Francisco, over 600 known disorders of the nervous system exist, which is why an entire class of medical specialists, known as neurologists, work to diagnose and – hopefully – treat such disorders. Biopharmaceutical companies are developing more than 400 new medicines to prevent and treat neurological disorders. Even though synthetic drugs are used for the management of Alzheimer's disease, Parkinson's disease, autism, and many other chronic illnesses, they are not without side effects. The attentions of researchers have been inclined towards the phytochemicals, many of which have minimal side effects. Phytochemicals are promising therapeutic agents because many phytochemicals have anti-inflammatory, antioxidative as well as anticholinesterase activities. Various drugs of either synthetic or natural origin applied in the treatment of brain disorders need to cross the BBB before they can be used. This paper covers various approaches of complementary and alternative medicine researches related to integrative medicine used in the management of neurodegenerative disorders.

Acute and chronic neurodegenerative diseases, including prion disease, frontotemporal dementia, Pick's disease, progressive supranuclear palsy, spinocerebellar ataxias, brain trauma, amyotrophic lateral sclerosis (ALS), Huntington's disease, Alzheimer's disease, and Parkinson's disease (PD), are illnesses associated with high morbidity and mortality rates [Prusiner,2001 & Friedlander,2003]. A characteristic of many neurodegenerative diseases is progressive neuronal cell death [Yuan & Yankner,2000]. During the past decade, considerable progress has been made in understanding the process of cell death [Hengartner, 2000]. The symptoms and the exacerbations of these diseases are much different according to their specific pathways of cell death, and having their own mechanisms of cell death leads to novel therapeutic strategies. Patients with neurological disease require special management considerations. These include pretreatment treatment planning, therapeutic techniques, and posttreatment requirements.

Today, there is no treatment that can cure degenerative diseases, but many symptomatic treatments are available. There are some advantages of Western medicines for these diseases, such as dopaminergic treatments for PD and movement disorders [Mizuno, 2014], cholinesterase inhibitors for cognitive disorders [Crane & Doody,2009], antipsychotic drugs for behavioral and psychological symptoms of dementia [Desai & Grossberg, 2005], analgesic drugs for pain [Chaudhuri & Schapira,2009], anti-inflammatories for infections [Tizabi et al.,2014],

and even the use of deep brain stimulation to stop tremor and refractory movement disorders [Okun,2014].

Researchers have also aimed to produce medicines to slow the development of diseases, such as Riluzole for ALS, cerebellar ataxia and Huntington's disease [Traynor et al 2006, Ristori et al,2010; Armstrong & Miyasaki,2012], NSAIDs (non-steroidal anti-inflammatory drugs) for Alzheimer's disease [Stewart et al., 1997], and caffeine A2A receptor antagonists and CERE-120 (adeno-associated virus serotype 2-neurturin) for the neuroprotection of PD [Schwarzschild et al.,2003; Marks et al.,2008]. However, this has not yet progressed very well and there still remain too many problems to administrate the progressive and serious symptoms of these diseases [Mizuno, 2014].

Including Western medicine and traditional medicine, integrative medicine [Pan W, Zhou 2014] has its advantages in treating degenerative diseases. Integrative medicine aims to be 'integrative' or 'whole'; it does not only treat the acute symptoms of these diseases, but it also considers all of the related symptoms and tries to improve the quality of activity of daily life (ADL) for the patients [Pan & Zhou,2013]. Non-motor disorders is one refractory symptom of PD, such as sleep disorders, autonomic symptoms, neuropsychiatric symptoms, gastrointestinal symptoms, sensory symptoms, and other symptoms including non-motor fluctuations and fatigue [Chaudhuri & Schapira,2009]. Similarly, progressive ALS exhibits many symptoms and influences the ADL of ALS patients significantly. And, at later stages, as with many other degenerative diseases, patients will suffer from inflammation, expiratory dyspnea, dysphagia, akinesia, etc.

Western medicine, other integrative medicines have also demonstrated excellent results for the serious problems of many degenerative diseases. Pan et al. [2014, 2011, 2011] demonstrated that traditional Chinese medicine (TCM) together with Western medicine can improve sleep disorders and other non-motor disorders of PD patients. Chua et

al. [2013] described the same effects of TCM on the quality of life when treating dyskinesias and non-motor symptoms in Chinese PD patients through a double-blind clinical study. Lloret et al. [2013] observed that Ayurveda medicine has a long history for the treatment of PD with fewer side effects. Pan et al. [2014] indicated in one of their studies that TCM can improve the behavioral and psychological symptoms of dementia in Alzheimer's disease. In another study [Pan et al. 2013], it is reported that TCM is not less effective than Riluzole in treating ALS, and moreover that TCM decoction can slow the development of ALS even more than Riluzole. Li et al. [2012] showed that the Tai Chi Quan can increase the stability of most PD patients. Most researchers aim at improving the ADL of degenerative disease patients by complementary and alternative medicine or integrative medicines [Kline,2002; Kum et al.,2011]. In recent years, researchers have also focused on increasing the ability of reserve to protect the mobility of degenerative disease patients by integrative medicine [Jiang & Pan, 2014]; we expect they will make some progress.

There are no effective treatments for degenerative diseases in modern society, but we can use Western medicine to deal with the acute disorders or symptoms and use the advantages of other integrative treatments to assist Western medicine in improving the ADL of the patients. Integrative medicine can, sometimes, exhibit protective effects or slow the morbidity of these diseases. It is believed that with the development of integrative medicine and modern science, the former will increasingly take a more and more important role in the treatment of degenerative diseases.

Conclusion: Since, Integrative medicine aims to be 'integrative' or 'whole'; it does not only treat the acute symptoms of these diseases, but it also considers all of the related symptoms and tries to improve the quality of activity of daily life (ADL) for the patients.

Acknowledgement: The corresponding author thank the UGC for granting financial assistance towards postdoctoral research under UGC PDFWM Scheme.

References :

1. Armstrong MJ, Miyasaki JM; American Academy of Neurology: Evidence-based guideline: pharmacologic treatment of chorea in Huntington disease: report of the guideline development subcommittee of the American Academy of Neurology. *Neurology* 2012;79:597-603.
2. Chaudhuri KR, Schapira AHV: Non-motor symptoms of Parkinson's disease: dopaminergic pathophysiology and treatment. *Lancet Neurol* 2009;8:464-474.
3. Chua K, Gao J, Kum W-F, Li M: The impact of treatment-related dyskinesias and non-motor symptoms on the quality of life in Chinese patients with idiopathic Parkinson's disease. *Int J Integr Med* 2013;1:31.
4. Crane PK, Doody RS: Donepezil treatment of patients with MCI: a 48-week randomized,

- placebo-controlled trial. *Neurology* 2009;73:1514-1515.
5. Desai AK, Grossberg GT: Diagnosis and treatment of Alzheimer's disease. *Neurology* 2005;64(suppl 3):S34-S39.
 6. Friedlander RM: Apoptosis and caspases in neurodegenerative diseases. *N Engl J Med* 2003;348:1365-1375.
 7. Hengartner MO: The biochemistry of apoptosis. *Nature* 2000;407:770-776.
 8. Jiang W, Pan W: Integrative cognitive reserve. *Integr Med Int* 2014;3:190-197.
 9. Kline KL: Complementary and alternative medicine for neurologic disorders. *Clin Tech Small Anim Pract* 2002;17:25-33.
 10. Kum WF, Durairajan SS, Bian ZX, et al: Treatment of idiopathic Parkinson's disease with traditional Chinese herbal medicine: a randomized placebo-controlled pilot clinical study. *Evid Based Complement Alternat Med* 2011;2011:724353.
 11. Mamta Prajapati, Smita Verma, *Assessment of Mine Effluents on Water Quality ; Life Sciences international Research Journal , ISSN 2347-8691, Volume 2 Issue 1 (2015), Pg 329-331*
 12. Li F, Harmer P, Fitzgerald K, et al: Tai chi and postural stability in patients with Parkinson's disease. *N Engl J Med* 2012;366:511-519.
 13. Lloret SP, Rey MV, Rascol O: Ayurveda medicine for the treatment of Parkinson's disease. *Int J Integr Med* 2013;1:6.
 14. Marks WJ Jr, Ostrem JL, Verhagen L, et al: Safety and tolerability of intraputamenal delivery of CERE-120 (adeno-associated virus serotype 2-neurturin) to patients with idiopathic Parkinson's disease: an open-label, phase I trial. *Lancet Neurol* 2008;7:400-408.
 15. Mizuno Y: Recent research progress in and future perspective on treatment of Parkinson's disease. *Integr Med Int* 2014;1:67-79.
 16. Okun MS: Deep-brain stimulation - entering the era of human neural-network modulation. *N Engl J Med* 2014;371:1369-1373.
 17. Pan W, Kwak S, Liu Y, et al: A compound belonging to traditional Chinese medicine improves nocturnal activity in Parkinson's disease. *Sleep Med* 2011;12:307-308.
 18. Pan W, Kwak S, Liu Y, et al: Traditional Chinese medicine improves activities of daily living in Parkinson's disease. *Parkinson Dis* 2011;2011:789506.
 19. Hanchinmani, C. N, Imamsaheb, S. J, Influence of Ga3 and Different Date of Sowing on Growth, Yield and Economics of Radish (*Raphanus Sativus*) ; *Life Sciences International Research Journal , ISSN 2347-8691, Volume 2 Issue 2 (2015): Pg 130-132*
 20. Pan W, Liu J, Wang Q, et al: Clinical study on chronic pain in Parkinson's disease patients in Shanghai, China. *Integr Med Int* 2014;1:93-101.
 21. Pan W, Su X, Bao J, et al: Open randomized clinical trial on JWSJZ decoction for the treatment of ALS patients. *Evid Based Complement Alternat Med* 2013;2013:347525.
 22. Pan W, Wang Q, Kwak S, et al: Shen-Zhi-Ling oral liquid improves behavioral and psychological symptoms of dementia in Alzheimer's disease. *Evid Based Complement Alternat Med* 2014;2014:913687.
 23. Pan W, Zhou H: Inclusion of integrative medicine in clinical practice. *Integr Med Int* 2014;1:1-4.
 24. Pan W, Zhou H: Integrative medicine: a paradigm shift in clinical practice. *Int J Integr Med* 2013;1:21.
 25. Prusiner SB: Shattuck lecture - neurodegenerative diseases and prions. *N Engl J Med* 2001;344:1516-1526.
 26. Ristori G, Romano S, Visconti A, et al: Riluzole in cerebellar ataxia: a randomized, double-blind, placebo-controlled pilot trial. *Neurology* 2010;74:839-845.
 27. Schwarzschild MA, Xu K, Oztas E, Petzer JP: Neuroprotection by caffeine and more specific A2A receptor antagonists in animal models of Parkinson's disease. *Neurology* 2003;61(suppl 6):S55-S61.
 28. Stewart WF, Kawas C, Corrada M, Metter EJ: Risk of Alzheimer's disease and duration of NSAID use. *Neurology* 1997;48:626-632.
 29. Tizabi Y, Hurley LL, Qualls Z, Akinfiresoye L: Relevance of the anti-inflammatory properties of curcumin in neurodegenerative diseases and depression. *Molecules* 2014;19:20864-20879.
 30. Traynor BJ, Bruijn L, Conwit R, et al: Neuroprotective agents for clinical trials in ALS: a systematic assessment. *Neurology* 2006;67:20-27.
 31. Yuan J, Yankner BA: Apoptosis in the nervous system. *Nature* 2000;407:802-809.

Dr. Swaroopa. Maralla, Post Doc Fellow in Biomedicine, Division of Zoology, Department of Sericulture, Sri Padmavati Mahila University, Tirupati-517502, Andhra Pradesh, India.

D. Bharathi,

Professor, Department of Sericulture, Sri Padmavati Mahila University, Tirupati-517502, Andhra Pradesh, India.