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An Update on Recent Advances in the Management of Neurological Disorders

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ABSTRACT

An increasing number of patients are being diagnosed with neurological disorders. Alzheimer's, multiple sclerosis and other neurological disorder of the brain affect one in six people around the world, driving a demand for innovative solution. Moreover, the cost and incidence of neurological disorders is expected to increase as the population age 65 and over is projected nearly double by 2050. Currently, there is no effective treatment for neurological disorders now it is important than ever to find advance treatment that both modify and prevent neurological disease. This review discusses recent advance in the management of neurological diseases such as Alzheimer's disease, Parkinson's disease, Stroke and Epilepsy.

INTRODUCTION

Neurological disorders is a state of progressive neuron dysfunction and death, which affects central peripheral nervous system. There are more than 600 neurological disorders such as Alzheimer's disease, amyotrophic lateral sclerosis (ALS), attention-deficit/hyperactivity disorder, brain injury, brain tumors, epilepsy, genetic disorders, headache, Huntington's disease, multiple sclerosis, muscular dystrophy, Parkinson's disease, spasticity, spinal cord injury, stroke etc. The factors which leads to neurological disorders are injuries, infection, environmental factors, poor nutrition exposure to heavy metals, gene changes, change in gene will leads to change the coordination between brain spinal cord and others. A recent report indicates that by US pharmacist 20 million Americans having neuropathy, 16%UShouse holds experiencing brain impairment. In each year 1.2million mostly diagnosed adult onset brain disorders 51.3% and 21% are caused by shock and Alzheimer's disorders. The total number of newly diagnosed episodes of Parkinson's diseases and traumatic brain injury equals the total number of epilepsy episodes (135 million). According to central brain tumor rigidity registry of US report in 2018, the total estimated number of new cases of brain and central nervous system disorders in US is 85440 and 86970 in 2018 and 2019 respectively.

An increasing number of patient's are being diagnosed with neurological disorders but are rarely cured because of the lack of better therapeutic treatment. There are numerous challenges are associated with management of neurological disorders such as poor knowledge about mechanism of action, lack of specificity in diagnosis, lack of efficient treatment, the limited regenerative capability of adult newer cells especially in central nervous system and lack of effective administration of certain drugs such as drugs which does not cross blood brain barrier efficiently in to brain. Early diagnosis of neurological disorders is still lack of high specificity and therapeutic outcome. The treatment is just symptomatic, so neurological disorders are still not curable. For advanced therapy use of nanotechnology based drug delivery system, bioimaging strategy, use of biomarkers, molecular targeting, personalized medicine, advanced biosensing techniques. Development of integrated methods to measure non motor symptoms help identification and development of better treatment strategy. The treatment of neurological disorders requires physical support to guide the growth and differentiation of nerve cells, swell as Nanocarriers to facilitate delivery of drugs. Neuroprotective agents and growth factors to cross blood brain barrier and to provide target to disease state.

To achieve the above demands for the earliest diagnosis and treatment of neurological disorders increasing efforts are being taken for the development advanced biomaterials, development of gene therapy and use of nanotechnology are developed. The proper design of drug delivery systems is required to distribute drug for the targeted site without affecting healthy tissue and cells. This review focusing on recent update on advanced management of neurological disorder to produce site specific and targeted drug delivery.

NEUROLOGICAL DISORDERS

Neurological disorders are diseases of central nervous system and peripheral nervous system. In other words, the brain, cranial nerves, peripheral nerves, nerve roots, autonomic nervous system, neuromuscular junction and muscle. The nervous system controlling the sensory input and motor output of the entire body. It is divided into central nervous system and peripheral nervous system. At cellular level nervous system mainly divided in to two main type of cells, Neurons and their support known as glial cells. In neurons there is protective connective tissue called Myelin sheath, to conduct rapid electrochemical signals and to release neurotransmitters such as acetylcholine, dopamine and glutamate. It will regulate the activation of glands and muscles via synapse. Neurological disease described as the disease of CNS disorder that is any abnormalities in structural, biochemical or electrochemical nature of brain, spinal cord or other peripheral nerves it results into severe range of symptoms with high mortality, morbidity and disability. These are modified when an increased free radical production leading to abnormal protein aggregates and oxidative injury. Neurological disorders include Alzheimer's disease, Parkinson disease, Multiple's disease, Epilepsy and other contributed disease [1].

ESTIMATES OF DEATH:

Neurological disease constitute 12% of total death globally (Table: 1.1). In lower income countries neurological disease constitute 16.8% of total death wherein high income countries it is 13.2% [2].

Table No. 1.1: Percentage of total DALYs for selected diseases and neurological disorders;

Selected Diseases	% of total DALYs
Neurological disease	6.3%
Tuberculosis	2.2%
HIV/AIDS	5.6%
Malignant neoplasms	5.3%
Ischaemic heart disease	4.1%
Respiratory disease	4.0%
Digestive disease	3.0%

ALZHEIMER'S DISEASE:

Alzheimer's disease is a neurological disorder results into cognitive behavioural impairment. It is the most common cause of dementia. AD is mainly due to the formation of plaque in hippocampus, a structure deep into brain that encode memories and used in decision making and thinking. In US the AD is the sixth leading cause of death it is estimated that 5.8 million of people are suffering from AD. In between 2000 and 2010 there is 68% increase in death due to AD. Death from heart diseases, stroke and HIV are increased 16%, 23% and 46% respectively. Unless medical breakthrough are made to prevent, retard or stop the disease progression, by 2050 the number of people aged 65 year old with AD nearly increased up to 13.8 million. AD recognized as one of the important medical problem in elder patients. Over time, the disease progress neuron in other region of the brain get destroyed as a result the individuals cannot perform every activities [3].

Pharmacological Treatment:

1. Cholinesterase inhibitors

According to cholinergic hypothesis of AD, basal forebrain are affected in the early stages including loss of acetylcholine neurons, loss of ach synthesis and its degradation resulting into progressive memory loss and other cognitive deficits. Cholinesterase inhibitors can enhance cholinergic transmission to delay the degradation of acetylcholine between the synaptic cleft has been proposed. Donepezil, Rivastigmine, Galantamine are the three drugs approved for AD. In addition, Donepezil is approved for severe AD in USA. In review

showed that incidence of GI side effects such as vomiting, diarrhoea and abdominal cramp was lower with donepezil compared to other drugs approved for AD.

2. N methyl D aspartate Antagonist

Memantine is the further therapeutic option for moderate to severe AD. It is believed to protect neurons from excitotoxicity. Memantine is an uncompetitive and having moderate affinity and reduce behavioural and psychological symptoms of dementia and improvement in cognition. The most frequently reported side effect associated with memantine is headache, dizziness and confusion, in some cases agitation also.

Recent advance in the treatment of AD

1. Disease modifying approaches to Alzheimer's disease

The production of Aβ, which is an important step in AD pathogenesis, is the result of the cleavage of APP, which is expressed in AD too much. Aβ and tau are principal targets for disease-modifying therapies in AD. From this point of view, AD could be effectively prevented or treated by reducing the production of Aβ and tau; prevent the aggregation or misfolding of these proteins; neutralize or eliminate the toxic aggregate or a combination of these.

2. Disease-modifying treatments: modulation of inflammation and oxidative damage

Epidemiological evidence suggests that long-term use of NSAIDs protects against the development of AD. Despite this premise, prospective studies have shown a lack of efficacy or a treatment limiting gastrointestinal toxicity and Potential antioxidants include mitoquinone, vitamin E, Ginkgo biloba, natural polyphenols such as green tea, wine, blueberries and curcumin, gras3 fatty acids, folate, vitamin B6, and vitamin B12 supplementation can slow the rate of cognitive decline in people with AD. In addition, the authors were impressed by the striking speed with which these improvements occurred in the study patients. Nevertheless, etanercept merits further study in RCTs [4].

3. Nanotechnology-based drug delivery systems for the Alzheimer's disease

Nanotechnology processing methods, which involve the design, characterization, production and application of drug delivery systems at the nanoscale, have been used to optimize therapy. These nanotechnologies include polymer nanoparticles, solid lipid nanoparticles,

nanostructured lipid supports, microemulsion, nanoemulsion and liquid crystals. Each of these tools holds promise for delivering therapeutic devices to the brain via different routes of administration, particularly the intranasal route. The objective of this study is to present a systematic review of drug delivery systems based on nanotechnology for the treatment of Alzheimer's disease. Polymer NPs, Liposomes, Surfactant-based systems are used for targeted drug delivery [5].

4. Radiation and Alzheimer's disease

Increased use of X-ray computed tomography (CT) for medical diagnosis and radiation therapy, risks of frequent theft, exploration of living space and possible radiological terrorism, research on ionizing radiation at low dose/dose rate becomes much more imperative and urgent than ever. Further study on lifetime monitoring of the radiation effect in individuals exposed to low dose or low flow may still be necessary to establish a close relationship between radiation exposure and the development of Alzheimer's disease [6].

5. Statins in Alzheimer's disease

Elevated cholesterol levels and the consequent presence of atherosclerosis have been shown to correlate with an increased risk of AD. In animal models, high doses of dietary cholesterol are associated with increased intra-neuronal-amyloid deposits and diffuse amyloid plaque formation, with regression of these lesions when cholesterol is removed from the diet. The apoE4 allele of the apolipoprotein E gene has been associated with high cholesterol levels and an increased risk of AD as well. Clearly, before cholesterol-lowering therapies can be advocated for AD, data from randomized clinical trials is needed to ensure that a true treatment effect is present and that the potential negative cognitive effects of statins do not occur [7].

6. Neuropeptides exert Neuroprotective effect in Alzheimer’s disease

Neuropeptides are molecules that work as endogenous active substances within the central nervous system and the peripheral nervous system. Neuropeptides play an important role in a wide range of brain functions, including food intake, metabolism, reproduction, social behaviour, reward, learning and memory, sleep and wakefulness. Recent studies have found that many neuropeptides, including ghrelin, neurotensin, pituitary adenylate cyclase activator polypeptide (PACAP), neuropeptide Y, substance P, and orxin, may be associated with

pathophysiology and potential therapy. As neuropeptide and receptor levels may change before Aβ deposition and neuronal loss, as well as positively / negatively correlating with cognitive impairment, future studies would focus on the detection of neuropeptides as biomarkers in early diagnosis and evaluation of the treatment of Alzheimer's disease. In addition, for notable neuroprotective effects, more research is needed to explore the potential use of neuropeptides, particularly via a practical method of administration such as intranasal application, in the prevention and cure of Alzheimer's disease [8].

PARKINSON DISEASE

PD is the second most popular neurodegenerative disease after Alzheimer's disease. The prevalence is 1–2 / 1000. However, 1% of the elderly are affected because the incidence increases beyond 50 years. Most cases of PD are sporadic and are known as idiopathic PD. However, first-degree relatives of PD patients have a two to three times higher relative risk of developing PD. When motor symptoms appear, the absorption of putamen dopa is reduced by at least 35%. The relationship between the nigrostriatal dopaminergic system and the endogenous striatal dopamine levels, which are considerably depleted in symptomatic PD, is not yet fully understood. Parkinsonism has three cardinal motor symptoms: bradykinesia, stiffness and tremors [9].

Pharmacological Treatment:

In 1960, the lack of dopamine in the brains of patients with PD was discovered, and the first rationally derived therapy was introduced in neurology when the "miraculous" improvement of motor symptoms under therapy with intravenous L-Dopa, the barrier blood-brain-passing dopamine precursor, has been reported. Since then, generations of medical students have learned that the symptoms of PD are caused by a dopamine deficiency. L-Dopa remains the benchmark for all the multiple symptomatic therapies available for PD. Due to the short plasma half-life of L-Dopa (1 to 2 hours), repeated intake results in a pulsatile plasma profile. The L-Dopa effect can be improved and prolonged by the combination with peripheral inhibitors - (a) of the degrading enzyme L-DOPA-decarboxylase (i.e. benserazide, carbidopa - standard combination) and (b) degradation of the catechol-O-methyl transferase enzyme (COMT) (i.e. by adding the short-acting COMT inhibitor entacapone or the intermediate acting tolcapone) - or with centrally active inhibitors of the degrading enzyme monoamino oxidase B (MAO-B), such as selegiline or rasagiline. As an advanced therapeutic option, the

L-Dopa emulsion can be applied by an external pump via a percutaneous tube into the jejunal cavity in order to provide an almost constant continuous supply of L-Dopa to the blood and therefore to the CNS [10].

Recent Advance in the Treatment of Parkinson Disease:

1. New Developments in the Treatment of Parkinson's Disease

Given this situation, efforts over the past 20 years to develop new treatments for PD can be divided into two categories:(1) improve symptomatic therapy for (1a) motor and (1b) non-motor symptoms and (2) address the potential causes of PD, focusing on alpha-synuclein protein, its chemistry, its synthesis, its aggregation, its degradation and its interaction with other proteins in order to develop a treatment modifying the disease.

2. Improving symptomatic therapy available for motors Symptoms

Several drugs have recently been approved or are still being tested. These developments include the improvement of the pump device to infuse L-Dopa into the jejunal cavity and the approval of a long-acting L-Dopa (duration of action from 5 to 6 hours). Surprisingly, little information is available on its use in daily practice and no active comparative trial (for example against intrajunal infusion of L-Dopa or DBS) is in progress or in the planning stages in patients with PD with motor complications. To prolong and strengthen the action of L-Dopa, the new reversible MAO B inhibitor, safinamide by asserting that the compound also influences glutamatergic transmission and the long-term inhibitor COMT opicapone has been approved (both currently in Europe). A prolonged-release (24-hour long-acting) formulation of amantadine has recently been reported to significantly reduce the severity and extent of L-Dopa induced dyskinesia and also to reduce downtime.

3. New Developments in Symptomatic Therapy for Non-Motor Symptoms

In 2011, the International Movement Disorder Society published a comprehensive review of evidence-based medicine on the therapy of NMS from PD. On the one hand, it provides a deep orientation for how to deal with individual MSNs in PM. On the other hand, this review demonstrates the few prospective multicenter randomized clinical trials or active comparators on Class I and Class II medicine "existed until now for the treatment of NMS in PD - unlike many prospective multi centers tests on motor symptoms and motor complications. Since

then, increased efforts in this area have led to the approval of new therapies. For the treatment of dopa mimetic-induced psychosis in PD, pimavanserin reverse agonist 5HT2A has been approved in the United States; thus, for the first time, an alternative to the currently used antipsychotic compounds, quetiapine or clozapine, is available, although an active comparison trial between pimavanserin and, for example, clozapine is missing. For severe pain syndromes, the slow release preparation of oxycodone/naloxone has been successfully tested in PD.

4. Search for Parkinson's disease-modifying therapy delivers first results

The ultimate therapeutic challenge remains. Anyone who knows a patient with PD asks why there is no treatment that prevents the (at least) motor manifestation of PD. Already diagnosed PD patients and their families dream of treatment that can slow or even partially reverse the progression of this devastating disorder with all of its advanced motor and non-motor symptoms and complications. Two therapeutic strategies are currently being followed. The first is based on epidemiological results and large prospective clinical trials reporting a correlation between an occurrence or a reduced prevalence (or both) of PD and the consumption of compounds such as caffeine or nicotine [11].

5. Nanotechnology for Parkinson Disease

Nano-activated approaches have been reported for the administration of various neurotherapeutics for PD therapy. Some of them are discussed below. i) PLGA nanoparticles: Poly (lactic-co-glycolic acid) (PLGA) is one of the most widely used biodegradable polymers for the development of nanomedicines. PLGA has attracted considerable attention due to its properties such as biodegradability and biocompatibility, extended drug release, better interaction with biological materials and target specificity. Previously it was used for the administration of drugs from the nose to the brain. ii) Solid Lipid Nanoparticles: Solid lipid nanoparticles (SLN), the first generation of lipid NPs, have barely studied for i.m. administration of anti-parkinsonian agents. iii) Nanoemulsions and mucoadhesive nanoemulsions: Nanoemulsions (NE), due to their lipophilic nature and small cell size, are widely explored as a delivery system to improve absorption through the nasal mucosa. Addition of mucoadhesive agents such as polyelectrolyte polymers aids in the retention of the formulation on the nasal mucosa, thereby providing prolonged distribution of the drug to the olfactory region [12].

6. Gene therapy

Gene therapy was first described in 1972 as a means of "replacing bad DNA with good DNA". Gene therapy can be used to treat diseases by introducing therapeutic genes or by replacing, silencing or correcting defective genes. There are many different approaches, but the main strategy is to use non-replicating artificial viral vectors; mainly different serotypes of adeno-associated recombinant virus (AAV) or lentivirus. New gene delivery methods are under development and have been successfully used in mouse models of PD. In recent years, gene therapy has also been tested in several human clinical trials, it is expected that the gene therapy approach will gain ground in the years [13].

STROKE

Stroke is one of the most disastrous manifestations of two common diseases, atherosclerosis and hypertension. Stroke is the second leading cause of death in worldwide. It represents a major economic burden with a considerable impact on public health. Age is the most important risk factor for all types of stroke. For each successive decade after the age of 55, the stroke rate doubles for men and women. In fact, more than 80% of strokes occur in the elderly (people ≥ 65 years of age). The increased vulnerability of older adults to stroke is associated with changes in the aging brain, but also the higher prevalence of well-documented risk factors for stroke in older adults, such as hypertension, atrial fibrillation, carotid stenosis or cardiovascular disease [14].

Current Management

Management of acute stroke should begin with the assessment of the individual patient by recognizing the heterogeneity of the underlying vascular mechanisms and the extent of tissue damage. The initial priority is to maintain the cerebral perfusion as much as possible. Brain perfusion in acute stroke is often directly related to average blood pressure and any hypotension should be avoided. In some contexts, induced hypertension can acutely improve cerebral perfusion. Thrombolysis with tissue plasminogen activator IV (tPA) has been the mainstay of acute stroke treatment since the publication of the NINDS trial and subsequent FDA approval in 1996. Endovascular Therapy. For AIS patients with large proximal occlusion, the revascularization rates achieved by IV t - PA alone are lower than in patients with smaller arterial occlusion. Targeted endovascular revascularization therefore holds great promise for improving patient outcomes. Two non-randomized inferiority tests, SWIFT and

TREVO-2, compared the new stent-retriever technology to the old merci retriever technology in patients with AIS with major arterial occlusion treated within eight hours. Early surgical decompression, Perhaps the most effective treatment for reducing stroke mortality [15].

Recent Advance in the Treatment of Stroke:

1. New therapeutic strategies targeting the innate immune response and early inflammation after stroke

Ischemia induces the production of reactive oxygen species (ROS) from damaged brain cells, and ROS activates platelets and endothelial cells, resulting in microvascular occlusion. Oxidative stress and the inflammatory cascade modify the permeability of BBB and worsen the extravasation of leukocytes. Recently, ROS and regulators of their production have been implicated in the activation of infiltrating leukocytes and several molecules have been considered as activators of immune infiltrating cells in the ischemic brain. Because the brain is a sterile organ, pathogens derived from bacteria or viruses are totally lacking in the normal, ischemic brain. These endogenous molecules are called molecular danger patterns (DAMP) and are considered to be danger signals or alarm molecules that alert immune cells to the presence of damage to brain tissue.

2. Inflammatory and mediating cytokines

Activated infiltrating immune cells and damaged brain cells produce various cytokines and inflammatory mediators. IL1b is expressed in the ischemic brain within 30 minutes of ischemia-reperfusion. Recently, the previously unknown mechanism of IL-1b production and activation of caspase-1 mediated by inflammation has attracted particular attention. TNF-alpha is another essential cytokine involved in ischemic brain damage, it expressed in ischemic brain tissue within one hour of ischemia-reperfusion. It produce significant reduction in the disease [16].

3. Nondrug Therapeutics for the treatment of ischemic stroke

The lengthening of the treatment window for the administration of tPA can be achieved by non-drug therapies, in addition to pharmacological approaches. Gas therapy has also been studied for its potential as a connective therapy to alleviate the various complications associated with delayed treatment. Studies have shown that HBO can facilitate the integrity

of BBB by restricting the formation of reactive oxygen species and that MMP-9 facilitated damage to TJP in rats subjected to stroke [17].

4. Nanotechnology for stroke treatment

Perfluorocarbon nanoparticles: nanoscale molecular imaging agents must have a relatively long circulation half-life, be sensitive and selective with respect to the epitope of interest, have an improvement in contrast compared.1)Platinum nanoparticles: newer and more innovative nanoparticles have also received recent attention. Platinum nanoparticles have significantly improved motor function and reduced the volume of myocardial infarction in the cerebral cortex. Activation of MMP-9 after occlusion disrupted the external components of the neurovascular unit and this was greatly inhibited by the platinum nanoparticles, resulting in neurological improvements.2)Iron oxide nanoparticles: Superparamagnetic iron oxide nanoparticles (SPIO) have been used as contrast agents for MRI for many decades. and citrate-coated VSOP-C184 (VSPIO), which did not reveal any significant toxicity.3)Polymeric nanoparticles: Nanoparticles have also been used as delivery vehicles for drugs that have the potential to disrupt the tight junctions of endothelial cells in the brain microvessels that form the most restrictive BBB. One study reported the development of a drug delivery system composed of a polymer nanoparticle formulated from a biodegradable polymer [poly-D, L-lactide-co-glycolide (PLGA)] which can trap hydrophilic agents. In addition, this nanoparticle can penetrate cell membranes via endocytosis and deliver therapeutic agents into the cell cytoplasm [18].

5. Gene therapy

Gene therapy is a promising approach for the treatment of stroke and other cerebrovascular disease, although it may take several years to happen. Gene therapy could take place before a stroke (for example, to stabilize atherosclerotic plaques) and / or after a stroke (for example, to prevent vasospasm after subarachnoid haemorrhage [HSA] or to reduce damage to neurons by ischemic insult). We transferred the gene encoding the peptide linked to the vasoactive calcitonin gene via the cerebrospinal fluid and demonstrated an attenuation of the vasospasm after SAH. The transfer of neuroprotective genes or small RNAs that interfere with neurotoxic genes has good potential for ischemic stroke [19].

EPILEPSY

Epilepsy is a neurological disorder characterized by recurrent and unpredictable interruptions of normal brain function, called seizures. It is one of the most common chronic conditions affecting around 50 million people of all ages worldwide. The median lifetime prevalence of epilepsy was 5.8 per 1000 in developed countries and 15.4 per 1000 in developing countries. The median prevalence of active epilepsy despite treatment was 4.9 per 1,000 for developed countries and up to 12.7 per 1,000 for developing countries. This has shown that the prevalence of epilepsy is higher in developing countries than in developed countries. In Asia, the median lifetime prevalence is estimated at 6 per 1,000, which is lower than that of developing countries in other regions of the world [20].

Pharmacological Treatment:

The management of antiepileptic drugs is effective in controlling seizures in approximately 60 to 70% of individuals, although this is often done through an extended trial and a "popgun" pharmacy. Choosing the front-line officer is complex but important. Initial selection requires that the clinician consider the individual patient and their wishes. The need for therapeutic monitoring, the side effect profile, teratogenicity and even cost are all important considerations, but the end goal is usually to achieve rapid and effective seizure control with minimal side effects. A large randomized controlled trial (the SANAD study) studied the drug of choice for newly diagnosed epilepsy of the generalized or partial seizure type. This study received a lot of attention and despite its high power and good follow-up, it was the subject of in-depth criticism, mainly for the lack of syndromic classification and its lack of blindness. The results, if accepted, suggest sodium valproate as the first line for generalized seizures and lamotrigine for partial seizures. In particular, there have been three new antiepileptics released since the start of this study (levetiracetam, zonisamide and pregabalin) and these are obviously not taken into account. The final choices of pharmacological agent are generally made individually and there is no universally accepted algorithm for therapeutic management [21].

Recent Advance in the Treatment of Epilepsy:

1. Gene transfer in epileptic disorders: the choice of "therapeutic" genes

An imbalance in excitatory and inhibitory neurotransmission is a widely recognized hypothesis for the hyperexcitability of the CNS underlying the epileptic state. Until now, therapeutic strategies have focused on the modulation of signalling mediated by the main excitatory and classic inhibitory neurotransmitters, glutamate and γ-aminobutyric acid (GABA). However, over the past 20 years, increasing attention has been paid to a group of bioactive peptides, including galanine and neuropeptide Y, which are abundantly expressed in the brain. It has become clear that peptides can also modulate neuronal excitability in a beneficial way to protect against seizures [22].

2. Nanotechnology used in the treatment of epilepsy

Nanoparticles can be as small as 10 nm and as large as 1000 nm and are generally composed of biodegradable polymers. Liposomes, polymers Stealth, targeting are widely used NPs for targeted drug delivery [23].

3. Epilepsy surgery

Epilepsy surgery allows 30% -40% of focal epilepsy patients to be discharged despite continued anti-epilepsy medications. Epilepsy surgery involves therapeutic research procedures, therapeutic techniques such as corpus colostomy and dissemination of impact devices. The purpose of pre-surgical assessment is to identify the epilepsy zone and prevent suboperative oncological and bowel deficiencies. However, epilepsy surgery is underused and should be considered for all patients with refractory focal epilepsy in whom two or three anti-epileptic drugs have been ineffective [24].

CONCLUSION

Neurological Diseases are the one of the leading causes of the death. Currently, there is no effective treatment for neurological disorders. So it is important to make innovative strategy to improve the status or treatment of neurological disorders. In this review detail discussed about the update advance therapy towards Alzheimer’s disease, Parkinson's disease, Stroke and Epilepsy. It include Nanotechnology based drug delivery, stem cell therapy, gene

therapy, combination therapy, surgical treatment, by using neuropeptides are mentioned. This therapies significally showing better result, but the complete cure is not achieved.

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