Review Article

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Neurodegenerative Dementias: A Brief Review

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Purpose: The purpose of this paper is to provide nurses with a concise review on neurodegenrative dementias. This review includes pathophysiology, clinical course, and tips on management of dementias from Alzheimer's disease (AD), Parkinson disease (PD) and lewy body dementia (LBD). Considering increasing numbers of dementia cases among older adults, nurses who are cognizant about dementia care are instrumental in maximizing daily activities and quality of life of patients with cognitive impairment and dementia.

Key Words: *Alzheimer's disease, dementia, Lewy body disease, Parkinson disease*
국문주요어: 알츠하이머병, 치매, 루이체병, 파킨슨병

INTRODUCTION

As the population ages, cognitive impairment and dementia also increase in older adults. Alzheimer's disease (AD) and Parkinson disease (PD) are the two most highly prevalent neurodegenerative diseases causing dementia. Lewy body dementia (LBD), another very frequent cause of dementia, clinically and pathologically resembles PD dementia but the onset of dementia is much earlier and the course more is aggressive in the former. Understanding the underlying mechanisms of cognitive impairment is a first step to better manage dementia. Since a cure for dementia is not yet available, mitigating impact on quality of life is a focus of nursing intervention. This paper provides useful dementia-related information including pathophysiology, differential diagnosis of neurodegenerative dementias and nurse management strategies for patient and family care. This review includes pathophysiology and management of AD, PD, and Lewy body dementias.

NEURODEGENERATIVE DEMENTIAS

Neurodegenerative diseases, defined as progressive death of neurons and supporting cells in the central nervous system, affect a large number of people nowadays and their incidence is increasing due to the aging population [1]. AD is the most highly prevalent neurodegenerative disorder, followed by PD [1]. Proteinopathy (the aggregation and accumulation of misfolded proteins) in specific brain regions is a hallmark of the neurodegenerative diseases [1]. Intracellular accumulation of tau and extracellular accumulation of amyloid β peptide are key features in AD, whereas intracellular accumulation of α-synuclein deposits called Lewy bodies is a key feature in PD and LBD [2]. Alpha-synuclein accumulation in the brain stem leads to disruption in production of a neurotransmitter called dopamine (this is controversial - alpha-synuclein may disrupt this but not necessarily lewy bodies themselves) [3]. Aggregated, oligomers or even monomers of amyloid beta or α-synuclein cause mitochondrial damage which trigger cellular death pathways [2]. Whereas, the key clinical symptom of AD is dementia, occurring about 60-80% cases, resting tremor, muscle rigidity, akinesia (bradykinesia), and postural instability (TRAP) are the primary motor manifestations of PD as a result of dopamine deficiency [4].

Although definitive AD diagnosis is confirmed by postmortem brain histopathology showing neuronal and synaptic loss and accumulation

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of amyloid beta plaques and neurofibrillary (tau) tangles, antemortem AD diagnosis rests on clinical guidelines supported by magnetic resonance imaging (MRI), position emission tomography (PET), or cerebrospinal fluid (CSF) of amyloid β and tau deposits [5]. Similarly, the diagnosis of PD is based on clinical history and neurologic examination supported by demonstrating nigrostriatal denervation [6]. The presence of parkinsonism (bradykinesia plus tremor or rigidity) is the central and essential feature of clinical diagnosis of PD [7]. Postural instability is also a feature of PD but usually does not appear until later stage of PD. Thus, early postural instability is more likely to be a form of *atypical* parkinsonism [7]. A clear benefit from dopaminergic therapy is a supportive feature for confirming PD[7]. Almost all PD patients have non-motor symptoms, pain being one of the most frequent but ignored feature of the disease [8]. Understanding the different disease mechanisms, is a first step to managing dementias.

Cognitive impairment and dementia occur most commonly in neurodegenerative disorders. Neurodegenerative dementias such as AD dementia and LBD are two most common in the elderly, whereas dementias from traumatic brain injury and brain tumors are common among younger adults [9]. The trajectory of AD, abnormal extracellular Aβ and intracellular tau accumulation in the brain, precedes neurodegeneration, neuroinflammation, and impaired neuronal function leading to cognitive impairment [10]. Common feature of AD dementia is progressive memory impairment [9]. LBD is an umbrella term for "dementia with Lewy bodies (DLB)" and "Parkinson's disease dementia (PDD) and the 2nd most highly prevalent neurodegenerative disorder in people over age > 65 years old [11]." Both DLB and PDD share similar dementia symptoms (e.g., visual hallucinations, rapid eye movement (REM) sleep behavior disorder, fluctuations in cognition and attention, mood changes, one or more features of parkinsonism (i.e., bradykinesia, tremor at rest, or rigidity) but the symptoms appear in a different order depending on the location of Lewy bodies formation [11]. Visual hallucinations are highly prevalent (up to 80%) in DLB and commonly happen at night typically having false perceptions of people, children and animals [12]. A REM-related parasomnia is physically acting out (movement or vocalization) dream content[12].

Parkinsonism occurs in over 85% of patients with DLB [12]. In DLB, dementia always appears first or around the time motor symptoms of Parkinsonism appear, whereas dementia appears after several years of motor symptoms of parkinsonism in PDD [11]. The features of dementia symptoms may help differentiate DLB from Alzheimer's dementia [11]. In addition, neuroimaging technique such as reduced dopamine transporter (DAT) uptake in single-photon emission computed tomography (SPECT) (DaT scan) or PET helps to differentiate DLB from AD [14].

DIAGNOSIS OF DEMENTIA

The diagnosis of dementia is largely based on thorough clinical history taking (both from patients and caregivers), interview focusing on the pace of symptom onset (e.g., sudden vs gradual) and symptom progression (e.g., decline over months or over years), neurological examination, and cognitive assessment utilizing tools such as the Montreal Cognitive Assessment (MOCA), the Cognitive Abilities Screening Instrument (CASI), and the Mini Mental State Examination (MMSE) [9]. Selective labs to screen metabolic/ physiologic abnormalities (e.g., basic chemistries, thyroid panel, B12, Vitamin D) and a structural brain scan such as MRI can be considered to aid in the diagnosis [9]. The MOCA is a commonly used reliable cognitive screening instrument (internal consistency = .83) [15,16]. The MOCA has 12 items measuring seven cognitive domains: executive functioning; visuospatial abilities; language; attention, concentration and working memory; abstract reasoning; memory and orientation[16]. It has a maximum of 30 point with a higher score representing better cognitive functioning [15]. A score of ≥ 26 (0-30 score range) in MOCA is considered cognitively intact. The CASI is also a widely used reliable (Cronbach's alpha > .90) cognitive assessment tool in patients with dementia [17,18]. The CASI was developed based on symptom profiles in the diagnosis of dementia and three cognitive measures (i.e., the Mini Mental State Examination, the Modified Mini-Mental State test, and the Hasegawa Dementia Screening Scale). It has nine cognitive domains such as long-term memory, short-term memory, attention, mental manipulation, orientation, abstraction and judgment, language, visual construction, and list-generating fluency [18]. A score of ≥ 86 in CASI is considered cognitively intact (0-100 score range).

MANAGEMENT OF DEMENTIA

Gingko biloba, vitamin B12 and folate, estrogens, anti-inflammatory drugs and statins have been popularized for the treatment of dementia but we do not have clear evidence for the effectiveness of these compounds thus these are not recommended for routine use [19]. Limited

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studies reported beneficial effect of cognitive stimulation therapy and reminiscence therapy in mild-to-moderate dementia [20,21]. Mild cognitive impairment (MCI) is the symptomatic predementia stage on the continuum of cognitive decline [22] and thus early detection and monitoring are important to prevent its progression and allow the patient and family enough time to prepare and plan for the unknown future in aging [22]. The key criteria to differentiate MCI from *dementia* are independence in functional abilities (e.g., ADLs and IADLs) and lack of significant impairment in social or occupational functioning in the former [23]. Although we currently do not have any pharmacological therapy to slow progression to dementia or cure MCI, lifestyle modifications such as diet, exercise, and cognitive stimulation were found to be common sense strategies to maintain and delay cognitive impairment [22,24,25].

Currently approved pharmacological treatments for symptomatic management of AD dementia are cholinesterase-enzyme primarily responsible for synaptic recycling of acetylcholine in gray matter-inhibitors: donepezil (Aricept®), rivastigmine (Exelon), and galantamine (Razadyne) and a neuron protecting agent against glutamate excitotoxicity: memantine (Namenda) [26,27]. Both 5 mg and 10 mg daily dosing of donepezil was found effective for AD dementia: start with an initial dose 5 mg daily and increase after 1 month to maintenance dose 10 mg daily [27]. It also has oral sustained release 23 mg film-coated tablet [27]. Rivastigmine starts with an initial dose of 1.5mg twice a day with meals and increase by 3 mg daily every 2 weeks to maintenance dose of 6mg twice a day [27]. Initial dose of galantamine is 4mg twice a day increased by 8 mg daily every 4 weeks to maintenance dose of 12 mg twice a day. Memantine is started with 5mg daily in week 1, 5 mg twice a day in week 2, 10 mg every morning and 5 mg every bedtime in week 3, and 10 mg twice a day in Week 4 and after [27].

We do not have currently FDA approved medications for symptomatic treatment of DLB. Drugs used for other indications such as AD and PD such as cholinesterase inhibitors are often utilized [3]. Patients with DLB often have a poor prognosis, short lifespan and fast cognitive decline relative to patients with AD or PDD [3].

CONCLUSION

Cognitive impairment and dementia are highly prevalent and a growing social burden as aging population increases but so far only symptomatic treatment is available. While we are researching therapeutic regimens to prevent, slow down the progression, or treat dementia, maintaining maximum daily functioning and quality of life are major targets in dementia management. Patients with baseline cognitive impairment and MCI need to be monitored closely to prevent and delay its progression among older adults. In addition, families of patients with early stage dementia needs proper education and counseling to better prepare for the later stages of the disease. Nurses can play a vital role in performing cognitive assessment for early identification of cognitive impairment and to effect timely interventions for minimizing the impact of neurodegenerative dementias. Knowledge of the disease states will prepare them well for this critical role.

CONFLICT OF INTEREST

The authors declared no conflict of interest.

AUTHORSHIP

SMK and KP contributed to the conception of the work, drafting the article, critical revision of the article, and final approval of the version to be published.

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