Ophthalmology Clinics in Alzheimer's Disease

Subjects: Ophthalmology

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Alzheimer's disease (AD) is the leading cause of dementia, which is a growing public health concern. Although there is no curative treatment for established AD, early recognition and modification of the known risk factors can reduce both severity and the rate of progression. Currently, an early diagnosis of AD is rarely achieved, as there is no screening for AD. The cognitive decline in AD is gradual and often goes unnoticed by patients and caregivers, resulting in patients presenting at later stages of the disease. Primary care physicians (general practitioners in the UK) can administer a battery of tests for patients presenting with memory problems and cognitive impairment, however final diagnosis of AD is usually made by specialised tertiary level clinics. Recent studies suggest that in AD, visuospatial difficulties develop prior to the development of memory problems and screening for visuospatial difficulties may offer a tool to screen for early stage AD. AD and cataracts share common risk and predisposing factors, and the stage of cataract presentation for intervention has shifted dramatically with early cataract referral and surgical intervention becoming the norm. This presentation offers an ideal opportunity to administer a screening test for AD, and visuospatial tools can be administered at post-operative visits by eye clinics. Abnormal findings can be communicated to primary care physicians for further follow up and assessment, or possible interventions which modify risk factors such as diabetes, hypertension and obesity can be undertaken.

Keywords: Alzheimer's disease ; screening ; cataracts ; eye ; dementia

1. Overview of Alzheimer's Disease

The most common form of dementia, Alzheimer's disease (AD) is a progressive and debilitating condition. It is a growing public health concern nationally and globally as life expectancies increase in the UK and the wider developed world. 1.6 million people are predicted to have AD by 2040 in the UK alone while by 2050 there are expected to be 115 million cases of dementia worldwide, with AD accounting for between 60% and 70% of these[1][2]. Studies have identified that AD and cardiovascular diseases share common risk factors, which include diabetes, hypertension, obesity, smoking, physical inactivity and poor dietary habits [3][4][5]. Non-modifiable risk factors in AD include female gender and age, with age also affecting life expectancy in AD sufferers, as people who are diagnosed in their sixties and seventies may live between seven and ten years, whereas people in the nineties are only expected to live for three years.

Two major factors that contribute to AD's pathogenesis are excessive formation of soluble and insoluble amyloid beta aggregates and deposition of intracellular neurofibrillary tau protein tangles [6][7][8]. The general progression of the disease begins with soluble amyloid beta accumulation and insoluble amyloid deposition. The accumulation of these deposits is attributed to neuronal degeneration and synaptic dysfunction. Emerging evidence supports the theory that deranged intracellular protein metabolism of neurons may underpin the mechanism of neuronal degeneration. Intracellular proteins are constantly renewed, and misfolded proteins are eliminated by the ubiquitin-proteasome system. Faults in the ubiquitin–protease system due to genetic mutations and variabilities allows accumulation of abnormal intracellular proteins, and this has been proposed as a prime driver in the pathogenic mechanism of AD [9]. Eventually there can be a 50% loss of synapses and neurons in the hippocampus, and memory impairments develop. As the disease progresses, synaptic impairment and network disturbances cause wider cognitive dysfunction. In the early stages, short-term memory loss and visuospatial impairment is often present; over time this often causes disorientation, self-neglect, changes in behaviour and increased wandering and restlessness. As the disease progresses, debilitating symptoms including aphasia, lexical anomia, agnosia and executive function may develop [6].

At present, there is no curative treatment for AD. Acetylcholinesterase inhibitors (Donepezil, Rivastigmine, and Galantamine) and NMDA-receptor partial agonists (Memantine) may offer relief of some symptoms, however these therapies are not associated with gain in cognitive function [10][11]. As the current drugs show limited clinical benefits, several interventional studies have shifted focus to identifying at risk individuals of AD and advocating preventive measures to manage AD long term [10][11]. Given AD's multifactorial nature, it has been suggested that multidomain interventions could be an original and potentially effective way to deal with symptoms arising from AD [12].

2. Evidence for Benefits of Early Diagnosis of AD

Early diagnosis of AD may have significant benefits for patients, caregivers, healthcare professionals and society as a whole. For patients and caregivers, an early diagnosis may reduce uncertainty and anxiety, improve relationships and quality of life, offer the opportunity to come to terms with the diagnosis and seek support [13]. It may additionally help to avoid crises and is overall extremely relevant to the wellbeing of the individuals [14]. Studies indicate that AD patients generally prefer an early diagnosis and wish for diagnosis to be disclosed to themselves and relatives who may be affected by this news [15][16]. An early diagnosis while mental faculties are relatively intact will allow individuals to make decisions for their future and plan ahead before their capacities decline and facilitate better preparation from families and carers [17].

For healthcare professionals, improved diagnostic pathways may help to avoid “medical nomadism” which can be experienced during the diagnostic process, wherein patients present to various doctors with the same complaint over a short period of time [18]. For services, better workload planning and resource allocation were highlighted in a study that asked primary care practitioners (nurses and GPs), and there may be an increased ability to anticipate future demand.[19] A recent study also speculated that timely diagnosis may avoid prescription of medications that could worsen cognitive function, and suggested that newer and novel disease modifying therapies are likely to be lot more effective if they are initiated early in the course of the AD disease [15].

Institutionalisation of AD patients accounts for a large proportion of the total care costs of AD, and patients assessed and treated early remain in the community longer, reducing this financial burden [19]. A recent literature review examined studies and models that addressed economic benefits of early diagnosis and treatment, concluding that the cost of early diagnosis and early intervention will be offset by subsequent savings achieved from reduction in institutionalisation [15]. Although patients may still require admission to a residential or nursing home in the terminal phase of their disease, the overall length of time in care and therefore cost, would be reduced. A cost-benefit analysis performed in the U.S.A. indicated that net fiscal benefits may be optimised when patients receive an early diagnosis of AD and can consequently benefit from interventions such early pharmacological therapy, and respite for carers [20]. One study estimated that a theoretical reduction of 6%, 10%, and 20% in residential care home admission over the course of ten years would result in savings to UK society of approximately £150 million, £245 million, and £490 million, respectively [21][22]. In summation, this information suggests that the development of more tools and clinical pathways to improve early diagnosis could reduce the financial burden of AD.

3. Current Screening and Assessment for Dementia—A Brief Overview

Presently there is no mass screening for dementia, and at the primary healthcare level screening and assessment is undertaken by a general practitioner (GP). GPs may choose various tools depending on resources and time available with the patient. Assessment commonly begins with the “one-minute test”, which is a short conversation about memory with the patient, and is intended to illuminate a need for further, more detailed assessments. Another option is the “Mini-Cog test”, which requires a few minutes. Here patients are asked to memorise a short list of words, draw a clock face and then repeat the memorised words. If a full ten-minute consultation is available, the GPCOG (the General Practitioner Assessment of Cognition) is the most used measure, which is easy to administer and takes in the views of the carer or relative. Finally, a more extensive tool is the Montreal Cognitive Assessment (MOCA), which requires a fifteen-minute planned interview. This assesses different cognitive domains: attention, concentration, executive functions, memory, language, conceptual thinking, calculations, visuospatial skills and orientation. A single consultation may not suffice to make a diagnosis of dementia, and it is recommended to use cognition tools alongside a careful history, discussions with carers and relatives, examination and normal screening blood tests. This commonly allows diagnosis to be made in patients with a typical presentation of AD. If the presentation is more complex, referrals need to be made to specialist clinics such as memory or neurology clinics. Currently there are no extensive visuospatial tests administered by GPs in primary care for the purpose of dementia screening.

4. Visuospatial Function in Early AD

Broadly defined, visuospatial function requires identification, integration and analysis of space, in addition to processing visual form, details, structure and spatial relations [21]. It is commonly conceptualised in three components, visual perception, construction and visual memory [23].

Visuospatial skills are the use of vision in the perception of the objects in an environment, and the spatial relationships between them. Integration of visual information occurs via two processing streams that are distinct neural circuits, which project from the striate cortex to the posterior parietal (dorsal) or inferotemporal (ventral) cortices. The dorsal regions

process space-based “where” information, while the ventral regions process object-based “what” information [23][24]. Visuospatial dysfunction is thought to be among the earliest manifestations of AD and eventually goes on to affect between 20%–43% of patients. It manifests in a variety of impairments including dorsal stream functions like angle discrimination and motion perception, in addition to ventral stream functions such as facial discrimination and recognition of objects and colours [23][25]. Disturbances of functions like reading, visuospatial orientation and visual search strategies may also occur [24]. Mild impairment in this domain has been shown to be a strong predictor of progression to AD, and it has been suggested that a decline in visuospatial function may be present about five to six years before AD is diagnosed [26][27]. Visuospatial function may therefore be of potential use as a cognitive marker for the detection of AD before it has reached a clinical stage or setting [28]

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