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Editorial

Alzheimer's Disease: A Quest for Better Management

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Alzheimer's disease (AD) is a common cause of dementia. It has been and remains a significant challenge for the health care personnel across the globe. The number of people affected by the disease is expected to reach 106 million globally by 2050. The research progresses rapidly in the field of AD. In the absence of therapy, the concept of early diagnosis is promoted. This is because absence of therapy is not equivalent to absence of care. Care protocols are sorely needed to increase the quality of life for not only the patients, but the caregivers as well. Especially in patients with mild cognitive impairment, advanced directives are needed for the patient who can still consider their future. Extensive neuropsychological testing, structural and metabolic neuroimaging and csf biomarkers are frequent modalities used or soon expected to be available for use for the early detection. Eyes are said to be the windows to the brain. Modalities that help detect tau in the retina early may be a useful and inexpensive method for disease detection. Early detection has been propagated internationally. Projects like European Joint Action Alzheimer's Cooperative Valuation in Europe (ALOVE) and REACH II protocol have been undertaken to these effects. Still, diagnosis is most often made late.

It is a priority disease and search for cure or disease modifying agents till 2025 is a significant goal. Plaques and tangles, and their constituent amyloid beta and tau, served to provide information about the pathogenesis behind the dementias especially AD. In the last decade, Aβ-42 immunization was attempted. This was found to be effective in reducing brain amyloid. However, clinical improvement was not noted. This was probably due to persistence of the other components of neuronal inflammation such as tau, which form subsequently. There are trials underway such as Dominantly Inherited Alzheimer's Network, Alzheimer's Prevention Initiative trial, Anti Aβ Treatment in Asymptomatic Alzheimer's disease trial and other trials by US National Institutes of Health. The trials focus on anti-amyloid therapy which may prevent or delay Alzheimer's disease. However, prior trials with this group of medications like solanezumab and bapineuzumab had failed in achieving their goal. They however did show a small cognitive benefit in people with mild AD. Drugs like solnezumab, crenezumab, gantenerumab, aducanumab, beta secretase (BACE) inhibitor have thus been under trial.

Tau is expressed within neurons (intracellular) where it performs its function of microtubule stability. Over expression of tau may cause neuronal degeneration and cell death. In such instances, extracellular tau may be appreciated. This latter may affect cell signalling by interacting with cell receptors. Misfolded tau leads to abnormal aggregation that may form sheets spreading from cell to cell. Tau pathology may result in neuronal loss and cognitive decline. Blockage of propagation of tau from cell to cell and avoiding the initial formation of abnormal tau (phenylthiazolyl-hydrazides, rhodanines, anthraquinones, N-phenylamines have been tried) may act as potential targets for newer therapies. Therapy for tau clearance has also been a potential target (proteasomes and proteases).

Current treatments target neurotransmitter abnormalities. They do not affect the underlying aetiology. If the progress continues as expected, in 2025, a patient of AD will be treated with risk factor therapy and lifestyle modifications. The patient will undergo imaging, csf analysis, and a genetic study for the offsprings. As per the results, anti-amyloid, anti tau therapy may be initiated for the patient. Biomarkers and scans may be tested to monitor the therapy response. A suitable therapy or vaccine may be offered to those found at risk of developing AD at a later date.

Such novel diagnostic modalities and treatment protocols would be welcomed across the globe by all healthcare personnel involved in management of Alzheimer's disease.

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