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Quality of Life among Alzheimer's cases in old ages & Actions that could be taken to prevent them

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Abstract:
More people will grow older, and especially in the 21th century with such great medical care, people's life expectancy increases. Imagine if there are 900 million elderly in the world, almost 100 million people, statistically, would eventually develop Alzheimer's disease (AD) AD. These diseases develop from a malfunction of two proteins in our body called the tau and the Amyloid-β. On that note, because AD currently still is an incurable disease, it is also important to make sure that the AD patients still have a healthy lifestyle in terms of their Quality of Life; the disease itself has had a serious impact on the patient's physical and mental health which we should not let any other element worsen their quality of life even more. This Literature review aims to scour the research papers available on Alzheimers' to list out some factors that reduce their mental welfare in AD patients. Our main claims are mainly looking at people with mild to moderate stages of AD who live alone where our references and data will be based on the particular group. Lastly, some people might claim that they have a deep understanding about AD, but in truth, we have little to no understanding about its origins and no proper treatments or therapies against them.

Keywords: Acetylcholine esterase inhibitors, Alzheimer's disease, dementia, depression, quality of life

Introduction

Alzheimer's disease, or AD is one of the progressive neurodegenerative diseases that occurs when a certain individual has a steady decline in terms of their abilities to remember something new, and their other cognitive abilities such as language, thought process, and organization (1-3). It's the most common type of Dementia which appears mostly in the elderly populations (4). Quality of Life (QoL) research on AD is considered a controversial topic because of how complex, subjective, and unpredictable it is (5). The study and measure of QoL is presumed that it can help explain the disease progression and the clinical meaningfulness of the changes (6, 7). This topic, in particular, is a crucial and essential consideration of AD from it's massive impact on the patients and caregiver because of its incurability and significant frequency in aging patients (8, 9). This study will aim to tackle the different factors that can affect the QoL in AD patients and caregivers, and ways to possibly benefit the QoL in their daily life.

Alzheimer's disease (AD):

Currently, in the scientific world, the Cause of AD is still an answer to look for. Although many case studies have pointed out some risk factors that could lead to the disease (10). These factors include age, family pedigree, apolipoprotein status, a concussion, depression casese, hypertension, health issues, low physical and cognitive activities, and more (11, 12). The Neuritic plaques and neurofibrillary tangles are the primary histological features of AD (7). The existence of phosphorylated protein tau (τ) is the characteristic of the former, and the buildup of the insoluble protein amyloid-β (Aβ) designates the latter

(13, 14). Both have been related to the severity of the clinical features of dementia syndrome (15, 16).

AD is a "neurodegenerative" and a PCD in short for "protein-conformational diseases" which is usually caused by the abnormal processing and polymerization of functional soluble proteins (15, 17, 18). When those proteins become misfolded, soluble proteins in the neurons will achieve a change in their structures, possibly due to allelic mutations, outside factors, aging, or aggregate which eventually leads to irregular neuronal functions (19, 20).

Ways to identify Alzheimer/ Dementia cases are done by using the Diagnostic or imaging approach. They require nanoparticle based detection to look for Alzheimer's biomarkers such as protein amyloid-β and Tau in cerebrospinal fluid samples collected from the patients (14, 21, 22). Nanomaterials can also be helpful as contrast agents for locating or scanning for aggregated amyloid-β plaques (16, 23, 24). It is crucial to comprehend the role of nanoparticles in increasing the effectiveness and the amount of the drug entering your blood circulation across the blood–brain barrier through until the central nervous system (25-27).

Treatment of AD:

NMDA or "N-methyl-D-aspartate" antagonist memantine are currently the only FDA-approved medications for AD patients (28, 29). Acetylcholinesterase inhibitors or AChEIs will attempt to decrease the decomposition of acetylcholine levels inside the brain of the AD patient (30, 31). This can be done by hindering the accountable enzymes in the synaptic cleft, the space that separates two neurons which are located between the presynaptic and postsynaptic endings (32, 33). Thus, AChEIs strengthen the central cholinergic neurotransmission and would ultimately diminish the decline in cognition at least for the first year of using this treatment. Further decline occurs, but even temporary discontinuation of these drugs will likely result in swift decline and is interconnected with an increase of risk in nursing home placement (34-36).

Initiation phase of the treatment is preferred as quick as possible after their AD diagnosis (2). Such patients, who started the AChEI 6 months later, are said to manifest greater cognitive decline compared to those who began taking the drug immediately. All 3 AChEIs have shown their ability in delaying cognitive decline, stabilizing, or even improving cognition of the patient's daily living in randomized placebo-controlled trials up to almost 52 weeks duration which is almost a year long (31, 36, 37).

Notable differences in drug effectiveness among the AChEIs have not been found yet (37). Also the 2 AChEIs, Donepezil and rivastigmine, have become FDA-approved for ranges from mild stages, moderate stages, until the severe stages of AD (38, 39). Meanwhile, galantamine, the other AChEIs, could only be used for mild stages and moderate stages of AD (40, 41). The most occurring side-effects are provoked by the cholinomimetic action from AChEIs on the gastrointestinal tract. These effects encompass diarrhea, waves of nausea, and emesis (42). Rapid Eye Movement (REM) in sleep behaviors have also been mentioned by some patients (31). Although, Taking the drug after breakfast is seen to prune all of the effects listed above (43). The transdermal patch of rivastigmine, a way you can administer the drugs without taking pills, might cause a rash at the location of the patch (20, 44). These side-effects affect nearly 5 percent to almost 20 percent of all patients but are mainly not so severe in those rare cases (20). The AChEIs may also trigger bradycardia, a decrease in heart rate, and increase the risk of fainting (20, 32). Thus, AChEIs are not suggested to be used in conditions involving patients with severe cardiac arrhythmias, especially bradycardia or syncope (fainting) (31). They should also be avoided in patients with active gastric ulcer or GI bleeding history and uncontrolled seizures (37). A slow and steady titration, or the process of observing of how your body is affected by the drug, for over months to years, is crucial for the well-being of the patients (1, 37).

Challenges for the treatment of AD:

Despite extensive research on the pathogenesis of AD over the last 30 years, little to no progress had been made in developing viable cures or techniques to prevent or treat disease (45, 46). With the tremendous increase in AD cases, society would face enormous economic and social challenges if no therapy is produced within the next couple of years (46-48). Moreover, it is worth noting that advancements in therapeutic techniques for AD that result in even minor delays in the emergence or progression of this

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disease will significantly reduce the disease's worldwide burden (49, 50).

Given the conceptual shift in the field over the last few years, Alzheimer's Disease is now considered a multidimensional process moving along a continuum rather than as discrete and defined clinical phases (51). According to expanding biomarker studies, it is increasingly understood that pathophysiological alterations in AD had begun many years prior to the clinical manifestations (41, 52, 53). For instance, it has been demonstrated that decreases in CSF tau levels occur 15 years prior to the onset of the clinical stages of this disease, although CSF A42 levels may decline even sooner, up to 20 years prior to symptom onset or appearance (21).

The clinical severity spectrum of this disease is ranging from showing little to no symptoms until severely impaired cognition (54). These borders, nevertheless, are challenging enough to establish, as the border between healthy aging adults and patients with preclinical AD is not well comprehended in our current medical knowledge and understanding (55, 56). This unanswered question is almost certainly going to be tackled in the near future, as early AD detection biomarkers have become a prominent area of research (22, 53, 56).

Differences in terms of gender should also be considered a biological variable in the pathogenesis of AD, as women account for approximately two-thirds of affected individuals (32, 57). The increased prevalence of AD in women may be, to a certain extent, accounted for by the fact that females usually live longer (57). However, even after accounting for women's longer lifespan than males, the risk of late-onset AD is more prominent in women (57). The biological mechanisms underlying women's more significant risk of developing AD remain unclear (28, 57). Nonetheless, it is now widely known that the shift from perimenopause onto menopause phase disturbs several systems regulated by estrogens, compromising multiple areas of cognitive function (58). Indeed, new preclinical research suggests that a shift in the brain's bioenergetic system in the course of menopause's beginning may act as an early beginning mechanism for expanded AD risk in the female brain (59, 60). These variables may promote fatty acid catabolism (61). A deposition, and synaptic plasticity, all of which may trigger AD (18, 62). As a result, unsatisfactory clinical trial outcomes may be partly explained by metabolic differences between men and women (57). As a result, the research community should fully embrace proposals to include both-gendered animals in preclinical studies (58, 63).

During which the amyloid cascade concept has influenced research for the last two decades, the recent emphasis on disease-modifying medication development may be critical for developing techniques that disrupt the underlying disease processes (37). Combination pharmacotherapy may also provide benefits for AD therapy. This technique is beneficial against various diseases, like tuberculosis, HIVs or AIDS, cardiovascular disease, and even cancer (23, 25, 46). It can increase the potential of medications that are unsuccessful on their own but have synergistic or additive effects when combined (23, 63, 64).

Given the well-documented high failure rate of central nervous system-targeted drug development, initiatives aiming at repurposing already-marketed medications represent an intriguing possibility for speeding up drug discovery in AD (65, 66). Given that metabolic dysregulation appears to be a critical factor in AD and that a plethora of medications for metabolic disorders have already been approved for human use (5). Repurposing such substances may possibly have the potential to speed therapeutic development (5, 46). This is because preclinical toxicological, human welfare, tolerability, and also pharmacokinetic evaluations might be completed more quickly (38, 61, 67, 68). Impaired insulin signaling in the brain or insulin resistance appears to be a critical factor in the molecular etiology of sporadic AD (16, 51). Consequently, targeting brain insulin signaling with medications already approved for diabetes mellitus, such as insulin and therapies that enhance insulin sensitivity, may hasten their development to treat AD (61, 69). It is worth noting that several anti-diabetic agents have already been examined in currently ongoing clinical trials, including insulin, exenatide, and liraglutide (63, 69, 70).

Neuroinflammation, particularly at its onset, promotes a vicious cycle of microglial activation, pro-inflammatory factor release, and neuronal injury (33, 71). Additionally, inflammatory mechanisms such as those induced by TNF-α may be coordinated

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between the brain and the periphery, implying a relationship between AD and peripheral metabolic dysregulation (71, 72). The critical responsibility of neuroinflammation in AD is further underscored by discovering that immune receptor gene variations, particularly TREM2, are associated with an increased risk of developing AD (73, 74). A substantial body of research suggests that inflammation may be a therapeutic objective in Alzheimer's disease (75). Nonetheless, anti-inflammatory substances such as non-steroidal anti-inflammatory drugs or NSAIDs, peroxisome proliferator-activated receptor or PPAR activators, minocycline, and TNF signaling inhibitors have not yet produced exciting results (76-78). However, lifelong use of NSAIDs has been associated with a decreased risk of developing AD (63, 78).

Additional treatment techniques utilizing intravenous immunoglobulins and monoclonal antibodies are being evaluated, although results are not conclusive at this time (37, 79). These contradictory findings may be somewhat explained by anti-inflammatory medicines targeting generic rather than specific neuroinflammatory components in AD (27). That being said, understanding the potential for addressing inflammation in neurodegeneration will require identifying particular modulators of inflammation at early AD stages (80).

Factors affected quality of life of AD's patients:

Depression is a common comorbidity in patients with Alzheimer's disease. A study measured the factors linked with the distinct Quality of Life scores studied by an instrument called the QoL-AD, which includes the scores given by the AD patient, the caretaker, and the average score between both (81). Two factors seemed to be the indication. Depression and/or polypharmacy were the 2 factors to be connected with the patient's QoL-AD score and the caregiver score in our study (82). There was a study documented a connection between depression with the patient and caregiver QoL-AD ratings in a study of 111 individuals with AD, with depression associated with lower QoL. Several other studies have established a link between depression and reduced well-being in AD patients, regardless of whether the QoL was self-assessed or evaluated by their caretakers (82). Depression had the most significant effect on patient-reported QoL, because of it having the greatest coefficient (compared to other factors like polypharmacy and anxiety) (82). Concerning the caregiver's assessment, depressing patients was likewise indicated to significantly affect QoL, with a coefficient of the same intensity as caregiver load (82). These discoveries emphasize the critical nature of recognizing and dealing with depressive indicators in AD patients due to our findings. However, diagnosing depression can be challenging, as many depressive symptoms, such as apathy or low energy, might be mistaken for dementia symptoms (28). Thus, both healthcare experts and the patient's immediate entourage should pay special attention to these types of symptoms (28). While antidepressants may be effective in treating depression in older persons, they come with a risk of unpleasant effects due to some patients having multiple disorders at once (Comorbidity) or interactions between two separate drugs in the case of taking multiple drugs (83). As a result, mature adults often receive not-so-great antidepressant dosage or are medicated for an insufficiently long time (83). Nonpharmacological therapies such as psychotherapy, which refers to cognitive behavioral therapy, one of many psycho-social interventions, or through interpersonal psychotherapy, and therapeutic exercises are effective for lenient to moderate depression in people with severe dementia (28, 84).

Polypharmacy was affiliated with a decreasing HR-QoL on the caretaker score of the QoL-AD and was more frequently affiliated with a lower HRQoL on the AD patient assessment (35). Individual elements of the QoL-AD were analyzed, and it was discovered that polypharmacy was remarkably correlated with worse scores on the well-being in terms of the patient's physical health, which appeared in both AD patient and caregiver reports (1, 85, 86). This relationship makes sense, as the requirement for several medications is typically a result of multiple comorbidities, and the presence of such comorbid disorders has a significant impact on the patient's opinion of their health (1). Likewise, a guardian who observes their dear ones suffering from multiple comorbid conditions is very expected to give the patient a lower HRQoL rating (86). Comorbidities were quantified in our study by referring to the Charlson Comorbidity score, which was found to be unrelated to HRQoL (86). This might be because of

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the Charlson index's restricted ability to capture the whole spectrum of disorders in older people.

There has previously been evidence of a link between anxiety and HRQoL (86). Anxiety was associated with a worse HRQoL on the AD patient assessment, regardless of depression, but it was not the case with HRQoL on the caretaker assessment (48, 86). Individual QoL-AD items analysis revealed that anxiety was substantially associated with worse HRQoL on the emotions, recollection, and self-confidence items (87). Depression also affected the mood and memory ratings reported by patients (87). Concerning the caregiver assessment, factors like anxiety were shown to affect none of the categories; however, depression had a substantial effect on the same items, namely the patient's emotions, recollection, and self-confidence (87). Although caregivers may mistake anxiety symptoms may be mistaken for depression by caregivers, although they could have manifested prior to depression or even be indications of imminent depression (86). Anxiety is frequently associated with sleep difficulties, impatience, and even worrisome agitation (86). Thus, it does not count as a trivial symptom, particularly given that it can be effectively medicated with treatment and psychology-based techniques that assist the patient in expressing and externalizing their uneasiness (37).

There was also a substantial correlation between caregiver's burdens/tasks and QoL-AD score (86). Most patients living at home with AD are taken care of by an unofficial caregiver, typically one of the patient's families or acquaintances. This caregiver carries the burden, which is heavier as the condition worsens and increases the complexity when taking care of them (82, 86). It was demonstrated that caregivers of dementia patients have a less quality of life than caregivers of patients with other chronic conditions such as cancer. Additionally, it is well established that a person's QoL affects their efficiency in the workplace, as well as an increase in their absences at the workplace(82). Thus, it is probable that the caregiver's QoL affects the quality of care that a caregiver can provide for a patient with AD (86). The study demonstrated that caregiver burden affects the caregiver's perceptions of practically all QoL-AD items, most notably "connection with family" and "relationship with friends" (82). For an AD sufferer, their caretaker often links to their entourage (82). When a caregiver is burdened, he or she is less available to execute this critical function (82).

Additionally, caregiver load affected the criteria "capacity to engage in recreational activities" and "ability to perform household duties" (82, 88). Both of these factors are contingent upon the patient's ability for the initiation, and if the patient lacks initiation, the caregiver plays a critical part in encouraging the patient to engage in both of these realms of activity (86). An exhausted caregiver is likely to prefer to do housework independently rather than accompanying the patient and supervising the activities with kindness and good intent, likewise, for recreational activities. A critical function of the caretaker is to suggest relief activities to the patient or arrange for the patient to engage in those activities, whether by transporting the patient to day-care centers, for example. The caregiver burden also affected the mood item, which can be explained by looking at the fact that AD patients are frequently susceptible to the moods conveyed by their companions (86). If the caregiver is exhausted or sad, the patient is most likely to be mindful of this and may feel responsible for contributing to the stress, assuming the patient is aware of their sickness, as guilt is a prominent symptom of depression (82, 88). The caregiver's burden is minimally understood by the patient with AD, mainly as the condition develops, mainly owing to the caregiver's lack of expression toward his patient (82, 88, 89). The caregiver's burden is an internal embarrassment that he/she shares on request to his/her entourage and other carers who assist him/her in caring for the patient. The caregiver's load affects the patient indirectly by altering the link between how spontaneous and how satisfied they are in their exchanges, with the patient frequently retaining the scope to recognize them within the people who assists (89). AD's impaired sense of feelings disrupts this predominantly emotional exchange (89). For these reasons, even if the load is not seen directly by the patient, it affects the patient and any psycho-behavioural changes that may occur (89). As a result, assessing caregiver burden is critical in the administration of patients with AD, all the more so because caregiver load can be avoided by the establishment of structured assistance i.e. house nurses (89).

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Several prior studies examined the parameters relating with patient and caretaker assessments of QoL-AD (90). Several authors discovered inconsistencies between the patient's and caregiver's assessments of the elements linked with QoL (90). Certain authors indicated that behavioral issues affected the caregiver's score. The patient group was different compared to other studies because they included AD patients that currently are in long-term care provisions, and the caregivers examined were nurses and staff, not the patient's family members or loved ones (90). A study investigated the intensity of AD was connected with the patient's assessment of their quality of life. Chan's study enrolled individuals at various stages of Alzheimer's disease with MMSE scores that ranged from six to twenty-eight (90). In contrast, the study we used to pursue our conclusion enrolled only patients who fit the criteria for the population for which the QoL-AD instrument was accurately validated, namely those with mild stages to moderate stages of AD (2, 6).

Conclusion:

While our understanding of AD has advanced significantly in recent years, there is still an unmet need for effective therapies. The drugs now licensed for AD treatment are still not disease-modifying; instead, they provide mild and brief symptomatic relief. From our studies, Depression and polypharmacy were found to be 2 main factors affecting their quality of life in AD patients. Numerous restrictions must be considered in future research. The findings are limited to mild to moderate AD patients who live alone. As a result, the findings cannot be extrapolated to patients with severe AD or those who are institutionalized.

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