SCHOLARLY REVIEW

The Ethics of Prescribing Dementia Drugs under the NHS: Balancing Consent and Clinical Outcomes

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Abstract

Alzheimer's disease is the most common cause of dementia and one of the most devastating brain disorders suffered by the elderly. It can progressively affect patients cognitively and psychologically. Since the disease causes irreversible damage to the brain, various pharmacological treatments (galantamine, memantine, lecanemab) are used to slow down the progression of the disease and the decline of the patient's quality of life. However, the literature suggests that most treatments have shown more risks than benefits. This paper responds to the challenges by assessing the ethical implications of prescribing drugs that have a limited chance of improving the underlying condition. Many patients lacking capacity, such as dementia patients, have the right to use advance directives to communicate their wishes to the healthcare team in advance. Doctors in the UK also have to strictly adhere to the General Medical Council's principles to ensure decisions are made in the best interest of the patients. This paper argues that pharmacological intervention is not cost-effective, due to the various adverse drug reactions and the patient's declining quality of life. However, patients not using drugs will have a continuous progression in the severity of dementia symptoms, leading to a higher financial burden and increased demand for social care.

Keywords: dementia, Alzheimer's disease, advance directives, medical ethics, lecanemab, galantamine, memantine

Introduction

This review evaluates the risks, burdens and benefits of pharmacological intervention for dementia within the context of the British National Health Service (NHS). This paper attempts to make the decision-making process for prescribing drugs with various adverse reactions more transparent for patients and their families.

Methodology

This research was sourced from Google Scholar and PubMed; the paper utilises a qualitative thematic analysis to find commonalities between sources, all of which were published before February 28, 2023. Research was categorised using a qualitative thematic analysis method to find commonalities between sources.

Discussion

Alzheimer's Disease

Dementia is a decline in mental ability severe enough to interfere with daily life, including the decline in memory, reasoning or other thinking skills (Alzheimer's Association, n.d.).

Alzheimer's Disease (AD) is the most common form of irreversible dementia. It accounts for 60 - 80% dementia cases and affects an estimated 850,000 people in the United Kingdom (Alzheimer's Association, n.d.). AD is a degenerative brain disease that is caused by complex brain changes following cell damage. It is not a normal part of ageing and leads to the decline of cognitive abilities, especially remembering new information. AD is most common in people over the age of 65, and it affects slightly more women than men (Alzheimer's Association, n.d.). AD is also a progressive condition with no cure, as it leads to dementia symptoms that gradually worsen over time. However, there are medications to help relieve and slow down the progression of the condition (Alzheimer's Association, n.d.).

Pharmacological Treatments

There are three main pharmacological treatments targeted to Alzheimer's Disease: galantamine, memantine and lecanemab.

Galantamine (brand name Reminyl) is an acetylcholinesterase inhibitor which works by breaking down a substance acetylcholine in the brain, helping nerve cells communicate with each other. Galantamine is aimed at patients with symptoms of mild to moderate Alzheimer's disease (NHS, n.d.). It has proven efficiency in improving cognition, behaviour, activities of daily living, and global functioning (Onor et al., 2007). Adverse reactions are usually quite mild, including nausea and loss of appetite, and they occur in 20% of patients taking medication. It encourages a quick recovery time as patients usually get better after two weeks of taking the medication. (NHS, n.d.)

Memantine (brand name Namenda) is another type of treatment aimed at patients with moderate or severe Alzheimer's disease. It is especially suitable for those who cannot take or are unable to tolerate acetylcholinesterase inhibitors (NHS, n.d.). It works by decreasing abnormal activity in the brain by blocking the effects of an excessive amount of glutamate involved in brain functions, such as learning and memory (Ables, 2004). It improves the ability to think and remember or may slow the loss of these abilities in patients with Alzheimer's disease. However, memantine, like other drugs, cannot cure Alzheimer's Disease or prevent the loss of these abilities at some time in the future and symptoms may get gradually worse even with the medication. Adverse reactions are temporary and include headaches, dizziness and constipation (NHS, n.d.).

Lecanemab, also known as Leqembi, is a new drug in its Phase III clinical trial. It is an amyloid beta-directed antibody that targets a protein, amyloid ,which builds up in the brain in people with Alzheimer's (Li et al., 2016). It is aimed at patients with mild cognitive impairment or mild dementia associated with Alzheimer's disease (NHS, n.d.). It is the most successful drug observed and is proven to slow the rate of disease progression by about 20–30% after 18 months of treatment in patients with early Alzheimer's symptoms (Lecanemab, Memory and Aging Center, n.d.). The most common adverse reaction is an infusion-related reaction, such as flushing, chills,

fever, rash and body aches. Another adverse reaction is amyloid-related imaging abnormalities with edema, or fluid formation in the brain. Studies with lecanemab show substantially lower rates of adverse reactions than other similar drugs (MacMillan, 2023).

Ethics of Prescribing on behalf of Patients with Impaired Capacity

There are ethical issues surrounding the prescribing of patients with impaired capacity. Capacity is the ability of the individual to make an informed decision free of coercion. This emphasises that respect for patient autonomy is a central premise behind the concept of informed consent and shared decision-making. It also supports patients in their decision-making process to give consent to or refuse medical intervention based on their values and information provided by the clinicians. A patient is presumed to have capacity to give or withhold consent unless it can be shown that there are grounds for thinking he/she lacks sufficient capacity. However, a patient with more severe dementia will lack the capacity to give consent.

Doctors prescribing for patients without capacity must follow the provisions of the Mental Capacity Act 2005 (Mental Capacity Act, 2005). It suggests that a patient is presumed to have capacity to give or withhold consent unless it can be shown that there are grounds for thinking he/she lacks sufficient capacity. In the case of an AD patient where it is almost guaranteed that they would lose their capacity, patients can use an advance directive to enable an individual to refuse a specific type of treatment at some point in the future (i.e. advanced refusal). Advance directives make provision for the donor (the patient) to appoint the donee (the advocate) in advance to make decisions relating to their health. This becomes effective when the patient loses capacity, so they can control their care for as long as possible. However, this does not confer the power to give or withhold consent, though it does confer the right for the donee to be consulted. The Act also suggests that it is legitimate to withhold and withdraw treatment or make an advance refusal of treatment if providing treatment is unlikely to benefit the patient overall, or if treatment prolongs death or causes unnecessary suffering, but does not include the right to demand for particular treatment or the right to die (GMC, 2010).

Clinicians registered with the General Medical Council (GMC) have to adhere to the ethical standards to ensure that decisions made are within the patient's best interest. The GMC's seven principles of decision-making and consent help doctors meet the standard of ethical principles that underpin good practice. It emphasises that all patients have the right to be involved in decisions about their treatment and care and to make informed decisions if they can. The exchange of information between doctor and patient is also essential to good decision making. Doctors must be satisfied that they have a patient's consent or other valid authority before providing treatment or care. The benefits of a treatment that may prolong life, improve a patient's condition or manage their symptoms must be weighed against the burdens and risks for that patient, before you can reach a view about whether it could be in their interests (GMC, 2020).

Process of Decision-Making

The decision-making flowchart for treating patients with dementia is based on work done by Dr. Roger Worthington presented at an NHS workshop in 2020, subsequently published in Clinical Teacher (Worthington et al., 2020). This iteration is an interpretation of his decision-making process.

1. Establish what is known about the patient with consultation with the MDT and check to see if important information is missing.

2. Identify the ethical and legal considerations that arise with regard to clinical decisions needing to be made.

3. Consult with family members or carers to establish broad agreement on next steps.

4. Consider whether assumptions are being made.

5. Ensure all parties communicate with each other on a regular basis.

6. Identify risk, benefits, burdens associated with proposed course of action and discussing them with patient.

7. Check to see if alternate courses of action could be applicable to the case.

8. If necessary, consult clinical guidelines and seek legal advice before proceeding.

9. Try and ensure that current known patient wishes are being respected.

10. Once a decision has been made, make full, contemporaneous notes.

The Burdens of Pharmacological Intervention

The pharmacological treatments for dementia are designed to help delay the functional decline, but do not alter the course of the disease. Adverse drug reactions occur in up to 90% of patients with AD, and have a substantial impact on both patients and caregivers (Alzheimer's Society., n.d.). It is arguably unethical to treat AD patients with the medication due to their modest efficacy, high cost and little improvement in quality of life (Brenner, 2007).

Galantamine is a dual-reacting cholinergic treatment that improves cognitive performance and delays symptoms and caregiver stress. Although it is widely prescribed for AD patients, it has very high rates of treatment discontinuation and side effects; Jones et al. (2004) reported that 46% of galantamine-treated patients reported gastrointestinal adverse effects. It is also extremely costly and is estimated to cost 12 hundred dollars annually for one patient (NHS, n.d.). In comparison to the other treatments, its effects are more clinically relevant; Wilcock et al. (2000) found that two thirds of patients who received galantamine were judged to have improved or remained stable at six months. The side effects are also less severe with 92% of adverse reactions being mild to moderate in severity and only around 12% were serious adverse events. The results show galantamine is relatively successful in slowing the progression of functional decline in patients with mild to moderate AD and therefore also decreases the patient's need for care. However, the patient's quality of life will still decline from the high rates of adverse drug reactions.

Memantine is another pharmacological treatment that is approved worldwide for treating moderate-to-severe AD. Tampi & Dyck (2007) found that it made a small improvement on cognitive function, as no significant differences were observed with the addition of the treatment. Its open-label phase (the phase used to compare treatments or gather additional information about the long-term effects in the intended patient population) further shows it has no effect on the underlying progression of the disease and often the rate of change in patients with moderate to severe AD accelerates over time until a stage of severe disease is reached (Leber et al., 2006). It is also not cost effective at around 18 hundred dollars (NHS, n.d.). Memantine shows the best profile of acceptability, but comes with serious risk if you don't take it as prescribed as symptoms often get worse quickly (Blanco-Silvente et al., 2018). \The risks outweigh the benefits, providing a weak support for using memantine to treat patients with AD. This contrasts with the widespread use of memantine due to the lack of pharmacological alternatives for treating severe AD, leading to a significant burden on patients and their families and a considerable cost to society.

Of the three, lecanemab is the most successful in treating dementia and is likely to lead to a slowing in clinical decline from AD. Its Phase III AD clinical trial reported that it slowed the rate of cognitive decline by 27% in an 18-month study involving participants with early stage AD. It also has lower rates of adverse reactions with 21.3% of patients who received lecanemab having incidence of adverse events (U.S. Department of Health and Human Services., n.d.). However, it has the most severe adverse reaction as it often results in amyloid-related imaging abnormalities (ARIA) which may cause blood vessel leakiness leading to localised brain swelling and bleeding in the brain (Grabowski, 2023). It is also a new treatment so it is less accessible and there are less studies around its effect on memory and daily function. Lecanemab is also the only drug that is not approved by the National Institute for Health and Care Excellence (NICE), as only patients enrolled in the Phase III clinical trial will recieve it, so the costs are not covered by the National Health Service and patients have to pay around $26,500 per year in the USA for just the treatment alone (Grabowski, 2023). However, the cost for medication only accounts for 5% of the total cost of care for treated Alzheimer's patients (Alzheimer's Society, n.d.).

All patients in the UK have the right to choose not to use pharmacological treatments which would increase caregiver stress and time of nursing home placement. The NHS covers the cost for both the galantamine and memantine treatments with tax

payments, but does not cover the social care cost. The cost of dementia to the UK is currently £34.7 billion a year, which works out as an average annual cost of £100,000 per person with dementia. Two-thirds of this cost is currently being paid by people with dementia and their families or by selling the home of the patient, either in unpaid care or in paying for private social care. (NHS, n.d.)

Conclusion

The various benefits and risks of galatamine, memantine and lecanemab regarding Alzheimer's Disease range from relieving the psychological and behavioural symptoms of dementia to increasing the risk of other adverse drug treatments and decreasing the patient's quality of life. The best interest of the patient is ensured in accordance with medical ethics. Patients with capacity have the right of decision-making and refusing treatments, and patients without capacity can use advance directives to influence their course of treatment as long as possible if and when they lose capacity. Pharmacological intervention is not always cost effective if the risks outweigh the benefits. The symptoms usually get worse through the natural progression of the disease, but adverse reactions could impact on the quality of life with the expensive costs of both the treatments and the social care. However, without the use of the treatments, the condition of the AD will continue to deteriorate, leading to an increased demand for costly nursing homes and carers.

Acknowledgements

I would like to thank Dr. Roger Worthington, an independent researcher based in London, UK, for giving me instructions and support throughout researching about this topic and constructing this paper. This paper and the research would not have been possible without him and I truly appreciate his unique insights.

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