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Audit of Alzheimer's disease management from a tertiary hospital in Brunei Darussalam

Abstract

Background: Alzheimer's disease (AD) is the most common cause of dementia. Management of AD is dynamic and multidisciplinary, involving pharmacological and non-pharmacological interventions to manage patient's symptoms, prevent clinical decline and improve quality of life. This study aims to evaluate the standard of patient care provided for the management of AD.

Patients and methods: This was a retrospective clinical audit of patients in Brunei Darussalam, with the International Classification of Disease and related health problems, tenth revision (ICD-10) diagnosis of AD between 2019 and 2020.

Results: There was a total of 168 patients (68 males, 100 females). Their mean age was 79.5 years. Only half of the patients (n = 84) were advised on measures to take to slow down the progression of the disease, and less than half (49.1%) of eligible patients were offered cognitive stimulation therapy. 51.8% (n = 87) were referred to occupational therapists for assessment of activities of daily living. 113 patients (67.3%) were started on cognitive enhancers; of these, 92 were continued on these medications. Donepezil was the most common drug prescribed (n = 78). Only 44.2% (n = 50) of the 113 patients were maximized on their cognitive enhancer dose. 84.1% had documented follow-up evaluations on the effect of cognitive enhancers. 88 (52.4%) patients had behavioural and psychological symptoms of dementia (BPSD), of whom 64 (72.7%) received treatment, with quetiapine (n = 33, 51.6%) being the most prescribed drug.

Conclusions: There are still gaps between guidelines and practice; more effort is needed to improve achieving the standards of care for the management of AD in Brunei Darussalam.

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Keywords: Alzheimer's disease, Brunei Darussalam, cholinesterase inhibitors, dementia

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Introduction

Dementia is a debilitating illness that affects mainly older people. More than 55 million people are living with dementia at present, with Alzheimer's disease (AD) being the most common type of dementia [1]. As there is no cure, the treatment goals for dementia focus on impeding disease progression and improving patients' and family members' quality of life. Non-pharmacological therapies for AD management include providing advice to remain active and recommending activities to promote health, cognitive stimulation therapy (CST) and cognitive rehabilitation for mild to moderate dementia. Occupational therapy (OT) for assessment of function is also recommended to maintain and support independence in activities of daily living (ADLs) [2–4]. In terms of pharmacological treatment, acetylcholinesterase inhibitors (AChEI) such as donepezil, rivastigmine, and galantamine are recommended for mild to moderate AD, while memantine is advised for moderate AD who are intolerant or contraindicated to the AChEI, or severe AD [2].

Up to 97% of dementia patients experience behavioural and psychological symptoms of dementia (BPSD). This can be classified into five domains:

— cognitive (delusions, psychosis);
— motor (repetitive movements, physical aggression, wandering);
— verbal (verbal aggression, yelling, repetitive speech);
— emotional (depression, apathy, irritability, anxiety);
— vegetative (sleep disturbances and appetite changes).

Depression or apathy is the most common symptom, while one–third are reported to have agitation, delusions, and eccentric motor behaviour such as fidgeting or wandering. Management of BPSD involves treating discomfort, identifying social and environmental causes of distress, and ruling out other causes of acute unwellness. Trialling non-pharmacological approaches is required, and physical symptoms should be treated before starting pharmacological therapies. Antipsychotics may be considered if patients are a threat to themselves or others [2, 5, 6]. Antipsychotics should be used with caution as there is an associated increased risk of mortality among people with dementia, mainly due to cerebrovascular disease and infections [5]. These drugs do not improve a person's function or quality of life and should only be used for symptoms such as aggression or severe distress [5, 6]. While depression and anxiety occur in dementia syndromes, the National Institute for Health and Care Excellence (NICE) do not recommend antidepressants for mild to moderate depression, unless clinically indicated for concomitant mental disorder [2].

Management of AD is multifaceted, aiming to maintain the quality of life for both patients and their caregivers. Appropriate utilization of therapies may delay clinical decline and reduce hospitalization and care costs of AD. This audit aimed to evaluate the standards of care provided in Raja Isteri Pengiran Anak Saleha (RIPAS) Hospital, the main tertiary hospital in Brunei Darussalam, on the management of AD. The standards of care audited against were as follows:

1. Offer advice on approaches to slow down the progression of AD.
2. Offer CST to AD patients with mild to moderate dementia.
3. Offer OT input for ADL assessment and support.
4. Offer cognitive enhancers for eligible AD patients.
5. Optimize the dose of cognitive enhancers used towards the maximum dose tolerated.
6. Provide follow-up after starting therapy to assess for changes in cognitive symptoms.
7. Identify BPSD symptoms and documented indication if antipsychotics were prescribed.

Patients and methods

This was a retrospective audit of patients with an International Classification of Disease and related health problems, tenth revision (ICD-10) diagnosis of AD and either attended clinics for assessment of dementia under Geriatric Medicine, Psychiatry, or Neurology or was admitted to RIPAS Hospital, Brunei Darussalam between 2019 and 2020. The electronic clinical records of these patients were reviewed. Data extracted included age, gender, baseline mobility, and dementia severity using the clinical dementia rating (CDR) scale. Baseline mobility was classified as follows: independent, stick or one assist, walking frame or two assists, transfers only and bedbound or immobile. The CDR scale was scored from 0 (normal) to 3 (severe) based on history and clinical assessments of six domains — memory, orientation, judgment and problem-solving, community affairs, home and hobbies, and personal care. The notes were reviewed to identify whether advice was given to slow down AD progression, whether CST was offered, and whether referrals were made for OT assessment. Other data collected include the type of AChEI prescribed, doses, follow-up to monitor response to treatment, whether they had BPSD diagnosed by clinicians, and whether antipsychotics were prescribed. Data collected were entered into Microsoft Excel and analysed. The study was performed by the principles of the Declaration of Helsinki.

Results

There were 168 patients, 68 (40.5%) males and 100 (59.5%) females. The average age was 79.5 years. Table 1 summarizes the mobility and clinical dementia staging of the patients. In terms of non-pharmacological management, 84 (50%) of patients and/or their family members were advised on measures to take to slow down disease progression, 55 of 112 (49.1%) patients with mild to moderate dementia *i.e.* CDR scale 0–2, were offered CST, while 87 (51.8%) patients were referred to OT for ADL assessment. Table 2 shows the breakdown of documented ADL function based on clinical notes from the OT or clinicians. Among the 113 (67.3%) patients prescribed AChEI, 92 were still on the medications, while 21 patients had AChEI initiated but were subsequently discontinued. There were 12 patients considered for AChEI treatment but not prescribed, while 6 patients were offered AChEI, but refused by patient or family members (Figure 1).

Table 3 shows the breakdown of medications prescribed for the 113 patients. Among these, 50 (44.2%) were up-titrated to the maximum tolerated dose of medications. There were 95 (84.1%) who received follow-up to assess the effect of therapy on their cognitive status. Table 4 shows the follow-up outcomes

Table 1. Mobility and clinical dementia staging of the patients

Mobility	n (%)
Independent	78 (46.4)
Stick/1 assist	21 (12.5)
Frame/2 assist	9 (5.3)
Transfer	29 (17.3)
Immobile	31 (18.5)
Clinical Dementia Rating (CDR) scores	
0	6 (3.6)
0.5	20 (11.9)
1	39 (23.2)
2	47 (28.0)
3	56 (33.3)

Table 2. Number of patients reviewed by either OT or physicians for ADL assessments

	Feeding n (%)	Dressing n (%)	Bathing n (%)
Independent	78 (46.4)	67 (39.9)	67 (39.9)
Assisted	65 (38.7)	65 (38.7)	66 (39.3)
Not documented*	23 (13.7)	29 (17.3)	28 (16.7)
Not assessed**	2 (1.2)	7 (4.1)	7 (4.1)
	168 (100.0)	168 (100.0)	168 (100.0)

* Not documented — not seen by OT, also not mentioned by anyone on the activity; ** Not assessed — seen by OT but activity not assessed/ /documented

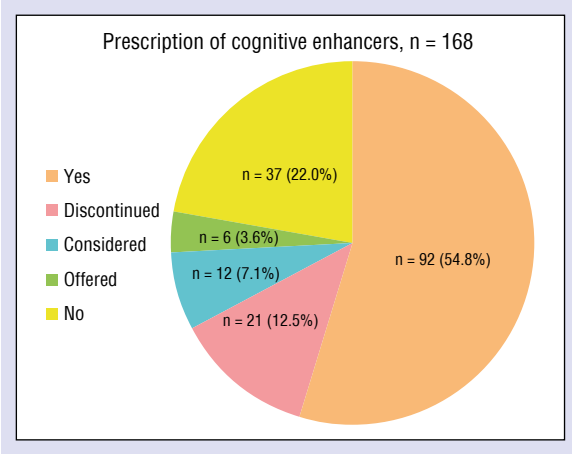

Figure 1. Number of patients on cognitive enhancers

Table 3. Types of cognitive enhancers prescribed to the 113 patients

Medication	n (%)
Donepezil	64 (56.6)
Rivastigmine tablet	28 (24.8)
Rivastigmine patch	3 (2.7)
Galantamine	1 (0.9)
Memantine	3 (2.7)
Tried both donepezil and rivastigmine (intolerant to one or both)	11 (9.7)
On both donepezil AND memantine	2 (1.8)
On donepezil (intolerant) → memantine	1 (0.9)

Table 4. Follow-up after starting cognitive enhancers from patients and/or family members

Effects	n (%)
Significant improvement	16 (14.2)
Slight improvement	13 (11.5)
No change	52 (46)
Worsened despite cognitive enhancers	14 (12.4)
No follow-up/documentation	18 (15.9)
Total	**113 (100)**

Table 5. Medications prescribed for BPSD (n = 64)

Medication	n (%)
Quetiapine	33 (51.6)
Risperidone	11 (17.2)
Sertraline	5 (7.8)
Olanzapine	4 (6.3)
Escitalopram	3 (4.7)
Amitriptyline	2 (3.1)
Fluoxetine	2 (3.1)
Fluvoxamine	2 (3.1)
Mirtazapine	1 (1.6)
Zuclopenthixol	1 (1.6)

after starting AD pharmacological therapy based on feedback from patients and/or family members. There were 88 patients with documented BPSD symptoms; among these, 64 (72.7%) were prescribed pharmacological treatment. Table 5 shows the medications prescribed for BPSD.

Discussion

For patients with Alzheimer's disease, clinicians should offer activities and promote independence and well-being to reduce the clinical progression of the disease and cognitive decline [2]. The World Health Organization (WHO) elaborated further on these recommendations; promoting physical activities, adopting a healthy balanced diet, maintaining social interactions, offering CST and better management of underlying hypertension, diabetes mellitus, and dyslipidaemia. Patients who smoke or drink alcohol should be advised on reduction, and eventually cessation [7]. The following audit indicated suboptimal (50%) counselling on measures to reduce disease progression, which needs to be improved. Patients and family members can be provided information leaflets during clinic visits and be reminded on subsequent follow-ups.

Cognitive stimulation therapy has been shown to benefit cognitive function and improve quality of life. It is a relatively inexpensive and cost-effective treatment for AD. CST was shown to be as effective as galantamine, and superior to rivastigmine and low-dose donepezil, with a 4-point improvement on the Alzheimer's Disease Assessment Scale — Cognition (ADAS-Cog), a measure for cognition. CST in addition to AChEI additively reduces the rate of disease progression [8]. However, it was found that less than half (49.1%) of mild to moderate AD patients and/or their family members were offered CST. It is also possible that not all those offered CST attended the sessions. The original CST trial was designed as a twice-weekly intervention, which may be difficult to travel to during the COVID-19 pandemic, where travel restrictions and social distancing rules were imposed. Some patients may not have been offered CST, as they may not be able to participate or find it distressing to carry out group activities. With the ease of COVID-19 restrictions, clinicians should advocate for and encourage patients to participate in CST during clinic consultations.

For ADL assessments, only 51.8% of AD patients were referred to OT for assessment and management interventions. This audit evaluated three selected domains: feeding, dressing and bathing. In the following settings, most patients referred from outpatient clinics will receive one initial consultation session, while hospitalized AD patients will receive daily or alternate days of therapy during admission. An Australian audit of 87 AD patients also reported underutilization of OT in the management of AD. It found that the common assessments done were home safety (48.3%) and fall risk (33.3%). Functional assessment was only done in 20.7% and personal care assessment in 2.3% of patients [4]. A German randomized controlled trial found that a single consultation for ADL assessment in AD patients was not inferior to ten community occupational therapy sessions [9]. Therefore, all AD patients should be referred to occupational therapy for at least a review of the home environment, function and personal care.

In this study, 67.3% of the AD patients received cognitive enhancers, which was similar to a study from China (64.1%) [10], and much higher in Germany (46.6%) [11], and Italy (20%) [12]. Finland reported an impressive record of 97% of AD patients on antidementia drugs [13]. A low prevalence of 16.1% use of cholinesterase inhibitors for AD patients in Brazil was noted [14]. Donepezil is the most prescribed (69%) AChEI in the following setting, similar to other studies [6, 14], probably due to its single daily dosing, cost, and milder gastrointestinal side effects [6]. Interestingly, rivastigmine was the most prescribed drug for AD patients in Brazil [14]. Donepezil is possibly the most cost-effective option among the AChEIs; while galantamine is slightly cheaper than donepezil, the quality adjust life years from donepezil is better and likely counterbalances the minimal cost difference [15]. A meta-analysis reported that donepezil, donepezil plus memantine, and galantamine were all effective medications for AD. However, donepezil was the only drug that reached a minimal clinically important difference threshold on the ADAS-Cog scale, hence is the

preferred drug choice for AD patients. The donepezil plus memantine combination used for severe AD carried a higher risk of side effects and was ranked least safe for headaches [16].

Multiple studies have demonstrated the dose--dependent efficacy of cognitive enhancers for AD, thus higher doses of AChEI are preferred to delay symptom progression in patients [17]. However, only 44.2% of the patients were trialled on the maximum dose of these drugs. Some patients may not tolerate higher doses due to gastrointestinal side effects, or adverse reactions such as bradycardia. Another possibility for up-titration failure was a lack of follow-up and monitoring of therapeutic effects after starting the medication. Thus, after starting the medications, changes in cognitive function should be evaluated. Ideally, measures for monitoring should be standardized; however, there are no locally validated tools for this purpose. Most follow-up to medication responses were documented in clinical case notes, while 15.9% did not have this documented at follow-up after starting therapy. Patients who experience improved cognitive symptoms should have their dose optimized, while patients whose symptoms worsened or remain unchanged should have a further reassessment of whether the drug should be continued, balanced against the risk of polypharmacy. A document template to record changes in symptoms may be useful, and if the person, family or caregivers are unable to attend, they should be given options to inform their clinician regarding responses to treatment. If unable to attend, family or caregiver may inform healthcare personnel through the designated hotline or e-mail.

More than half of the AD patients reported BPSD symptoms, with 72.7% of those with BPSD receiving pharmacological therapy. Quetiapine (51.6%) was the most prescribed, followed by risperidone (17.2%). Generally, antipsychotics, except for risperidone in some countries, are not authorized for managing BPSD. For patients with mild to moderate agitation, non-pharmacological interventions such as relaxation, improving surrounding environment and behavioural therapy should be attempted first. For severe agitation or aggression, risperidone is advised by two guidelines: 2018 CANADA and 2020 European Academy of Neurology (EAN) as first-line pharmacological treatment [18, 19]. Possible adverse effects of antipsychotics include weight gain, extrapyramidal symptoms, QT-prolongation, and drowsiness. There is also an increased risk of mortality, and cardiovascular and cerebrovascular complications, resulting in a black box warning for their use. Therefore, if required, the use of antipsychotics must be limited to the lowest dose and regularly re-evaluated for their benefits and risks to the patient [19].

Despite off-label use, quetiapine was the most common antipsychotic prescribed, similar to a study done in India, possibly due to its lower tendency of extrapyramidal symptoms, and as a preferred option for dementia with Parkinsonism [5, 19]. Antidepressants such as citalopram and sertraline were shown to improve agitation and aggression; however, the general consensus is that more research is required before coming to conclusions regarding their effects. There are also limited studies reviewing pharmacologic therapy for depression and apathy in dementia. However, selective serotonin reuptake inhibitors (SSRI) are generally the favoured treatment for depression, with a preference for sertraline and citalopram due to fewer drug-drug interactions [5].

There are several limitations of the study: it is a small study limited to AD patients seen in one hospital, thus findings may not be generalizable to other settings. There may be a bias towards more severe AD, as these were patients seen in a tertiary centre.

Conclusions

Management of AD is complex and requires a multidisciplinary team. The disease affects not only the patient but changes the lives of families and caregivers. This audit showed that there were still gaps between guidelines and practice, which requires further effort to achieve the standards of care for AD management. Recommendations to improve AD patients' care include providing patient information leaflets, promoting CST and offering OT assessment to patients during clinic reviews; re-evaluating medications periodically, i.e. up-titrating cognitive enhancers for them to achieve maximal potential effects, or stopping them if patients are deteriorating on it, and discontinuing antipsychotics in stable docile patients.

Article information and declarations

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None.

Data availability statement

The data that support the findings of this study are available from the corresponding author, (SPT), upon reasonable request.

Ethics statement

The study was performed in accordance with the principles of the Declaration of Helsinki.

Author contributions

Both authors were involved in conception, design, data analysis, drafting and finalising the manuscript. SYT did the data collection.

Conflict of interest

The authors have no conflicts of interest to declare.

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Supplementary material

None.

References

1. Dementia. World Health Organisation (WHO). https://www.who.int/news-room/fact-sheets/detail/dementia (20.12.2022).
2. Dementia: Assessment, management and support for people living with dementia and their carers. National Institute for Health and Care Excellence: Guidelines. 2018, indexed in Pubmed: 30011160.
3. Cameron I, Curran S, Newton P, et al. Use of donepezil for the treatment of mild — moderate Alzheimer's disease: an audit of the assessment and treatment of patients in routine clinical practice. Int J Geriatr Psychiatry. 2000; 15(10): 887–891, doi: 10.1002/1099-1166(200010)15:10<887::aid-gps212>3.0.co;2-m.
4. Rahja M, Comans T, Clemson L, et al. Are there missed opportunities for occupational therapy for people with dementia? An audit of practice in Australia. Aust Occup Ther J. 2018; 65(6): 565–574, doi: 10.1111/1440-1630.12514, indexed in Pubmed: 30187917.
5. Coak N, Al Khalili Y. Behavioral and psychological symptoms in dementia. StatPearls [Internet]. 2022.
6. Prasad K, Gupta H, Bharath S, et al. Clinical practice with antidementia and antipsychotic drugs: Audit from a geriatric clinic in India. Indian J Psychiatry. 2009; 51(4): 272–275, doi: 10.4103/0019-5545.58292, indexed in Pubmed: 20048452.
7. Risk Reduction of Cognitive Decline and Dementia: WHO Guidelines. 2019.
8. Spector A, Woods B, Orrell M. Cognitive stimulation for the treatment of Alzheimer's disease. Expert Rev Neurother. 2008; 8(5): 751–757, doi: 10.1586/14737175.8.5.751, indexed in Pubmed: 18457532.
9. Voigt-Radloff S, Graff M, Leonhart R, et al. A multicentre RCT on community occupational therapy in Alzheimer's disease: 10 sessions are not better than one consultation. BMJ Open. 2011; 1(1): e000096, doi: 10.1136/bmjopen-2011-000096, indexed in Pubmed: 22021760.
10. Yu L, Chen X, Yu Z. Trends of antidementia drugs use in outpatients with Alzheimer's disease in six major cities of China: 2012-2017. Int Clin Psychopharmacol. 2019; 34(6): 312–316, doi: 10.1097/YIC.0000000000000278, indexed in Pubmed: 31274694.
11. Hessmann P, Dodel R, Baum E, et al. Use of antidementia drugs in German patients with Alzheimer's disease. Int Clin Psychopharmacol. 2018; 33(2): 103–110, doi: 10.1097/YIC.0000000000000205, indexed in Pubmed: 29112517.
12. Franchi C, Lucca U, Tettamanti M, et al. Cholinesterase inhibitor use in Alzheimer's disease: the EPIFARM-Elderly Project. Pharmacoepidemiol Drug Saf. 2011; 20(5): 497–505, doi: 10.1002/pds.2124, indexed in Pubmed: 21432941.
13. Taipale H, Tanskanen A, Koponen M, et al. Antidementia drug use among community-dwelling individuals with Alzheimer's disease in Finland: a nationwide register-based study. Int Clin Psychopharmacol. 2014; 29(4): 216–223, doi: 10.1097/YIC.0000000000000032, indexed in Pubmed: 24608822.
14. Moraes FS, Souza ML, Lucchetti G, et al. Trends and disparities in the use of cholinesterase inhibitors to treat Alzheimer's disease dispensed by the Brazilian public health system — 2008 to 2014: a nation-wide analysis. Arq Neuropsiquiatr. 2018; 76(7): 444–451, doi: 10.1590/0004-282X20180064, indexed in Pubmed: 30066795.
15. Bond M, Rogers G, Peters J, et al. The effectiveness and cost-effectiveness of donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease (review of Technology Appraisal No. 111): a systematic review and economic model. Health Technol Assess. 2012; 16(21): 1–470, doi: 10.3310/hta16210, indexed in Pubmed: 22541366.
16. Tricco AC, Ashoor HM, Soobiah C, et al. Comparative effectiveness and safety of cognitive enhancers for treating alzheimer's disease: systematic review and network metaanalysis. J Am Geriatr Soc. 2018; 66(1): 170–178, doi: 10.1111/jgs.15069, indexed in Pubmed: 29131306.
17. Blesa R, Toriyama K, Ueda K, et al. Strategies for continued successful treatment in patients with alzheimer's disease: an overview of switching between pharmacological agents. Curr Alzheimer Res. 2018; 15(10): 964–974, doi: 10.2174/1567205015666180613112040, indexed in Pubmed: 29895249.
18. Ma H, Lu X, Zhou A, et al. Clinical practice guidelines for the management of behavioral and psychological symptoms of dementia: a systematic review with AGREE II. Front Neurol. 2022; 13: 699–723, doi: 10.3389/fneur.2022.799723, indexed in Pubmed: 35693007.
19. Tible OP, Riese F, Savaskan E, et al. Best practice in the management of behavioural and psychological symptoms of dementia. Ther Adv Neurol Disord. 2017; 10(8): 297–309, doi: 10.1177/1756285617712979, indexed in Pubmed: 28781611.