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[ORIGINAL ARTICLE]

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

[Short title: Alzheimer's disease management audit in Brunei]

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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. The aim of this study is 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 International Classification of Disease and related health problems, tenth revision (ICD-10) diagnosis of AD between 2019 and 2020.

Results: There were a total of 168 patients (68 males, 100 females). Their mean age was 79.5 years. Only half of the patients (n = 84) were given advice to slow down the progression of disease, and less than half (49.1%) of eligible patients were offered cognitive stimulation therapy. 51.8% (n = 87) were referred to occupational therapist 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 evaluation on the effect of cognitive enhancers. 88 (52.4%) patients had behavioral 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 management of AD in Brunei Darussalam.

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

Introduction

Dementia is a debilitating illness that affects mainly older people. There are more than 55 million people 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 behavioral 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 behavior 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. Trialing 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, reduce hospitalization and care costs of AD. The aim of this audit was 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 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 the dementia severity using the clinical dementia rating (CDR) scale. Baseline mobility was classified as follows: independent, stick or one assist, walking frame or two assist, 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 analyzed. The study was performed in accordance with 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 after starting AD pharmacological therapy based on feedback of patients and/or family members. There were 88 patients with documented BPSD symptoms; among these, with 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 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 dyslipidemia. Patients who smoke or drink alcohol should be advised on reduction, and eventually cessation [7]. Our audit indicated suboptimal (50%) counselling on measures to reduce disease progression, which needs to be improved on. Patients and family members can be provided information leaflets during clinic visits and be reminded on subsequent follow up.

Cognitive stimulation therapy has been shown to benefit cognitive function and improve quality of life. It is 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 reduce 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 our 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 the admission. An Australian audit of 87 AD patients also reported underutilization of OT in 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% 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 for the home environment, function and personal cares.

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% AD patients on antidiementia 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 our 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 adjusted 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 minimally clinical important difference threshold on ADAS-Cog scale, hence is the preferred drug choice for AD patients. The donepezil plus memantine combination used for severe AD, carry a higher risk of side effects, and was ranked least safe for headache [16].

Multiple studies have demonstrated 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 trialed 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 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. For patients who experience improved cognitive symptoms should have their dose optimized, while patients whose symptoms worsened or remain unchanged should have a further reassessment 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 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, with the exception of 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 behavioral 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, 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 of-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 is also limited studies reviewing pharmacologic therapy for depression and apathy in dementia. However, selective serotonin reuptake inhibitors (SSRI)

are generally the favored treatment for depression, with a preference for sertraline and citalopram due to less 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 center.

Conclusions

Management of AD is complex and requires a multidisciplinary team. The disease affects not only the patient, but changes the life 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 to patients during clinic reviews; re-evaluate 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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Data availability statement

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Ethics statement

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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.

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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

Table 3. Types of cognitive enhancer 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)

Figure 1. Number of patients on cognitive enhancers

