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Challenges of prescribing antidepressants for the elderly: a scoping review

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Abstract

Objectives With a shift in global demographic trends favouring the older population, depression, which is increasingly common to older adults, is fast becoming a significant public health phenomenon that can result in rising healthcare costs, co-morbidities and fatalities. In particular, challenges to prescribing antidepressants to older people given their altered pharmacodynamic and pharmacokinetic profiles is of major concern to healthcare providers. We aimed to review the challenges encountered by prescribers when diagnosing and selecting older patients suited to receive an antidepressant.

Methods English articles published between 2011 and 2021 were searched from the three databases which were MEDLINE, Cochrane Library and EMBASE to identify studies related to challenges in prescribing antidepressants for older people with the combination of search keywords such as depression, antidepressants, elderly and challenges, but not limited to them. Studies were excluded if the age of the participant is below 65 years old. The relevancy of the studies to be included were examined initially based on their titles and abstracts. Additional articles were searched from the reference lists of relevant articles.

Key findings Out of 2500 studies, 11 articles was included in this study. The challenges were classified into three themes: challenges associated with the ageing processes, difficulty in recognising depressive symptoms and challenges in distinguishing depression from cognitive impairment.

Conclusions Antidepressant prescribing in the elderly is complicated, in which there is a lack of proof for beneficial approaches. The study highlighted pertinent challenges to prescribers when older patients seek drug therapy for depression. This could have easily led to many depression cases gone undiagnosed or misdiagnosed.

Keywords: depression; mental health; pharmacotherapy; therapeutics; biomarker

Introduction

Depression can be described as persistent despair and a loss of enthusiasm or interest in previously pleasurable activity, according to the World Health Organization (WHO).[1] In the context of Asian countries, the prevalence of depressed older adults is between 12% and 34% in countries such as India (12.7%), Malaysia (16.5%), Vietnam (17.2%), Sri Lanka (27.8%), Japan (30.3%) and Indonesia (33.8%).[2–4]

With a global shift in demographic trends favouring the older population, clinicians are expecting to face more depressed older patients, in particular the young olds, rather than younger adults. In the era of the Covid-19 pandemic–endemic and with rising financial and psychosocial constraints, suicide is sadly significantly elevated in the depressed older adults, as is mortality from other diseases. WHO ranked depression as the single greatest contributor to global disabilities and also as the primary cause of death with an estimated figure close to 800 000 per year.[2]

Given the pronounced impact of depression and its associated suicide risks, and as more reports are made that the older people may not be getting the necessary treatment, we embarked to scope available literature and to evaluate the potential challenges to prescribing antidepressants for the vulnerable, older population.[4, 5]

Methods

Search strategy

Studies that were published between 2011 and 2021 were retrieved from the following electronic databases: MEDLINE, Cochrane Library and EMBASE.

The search terms were grouped into three main categories. Each category was then combined by using the Boolean operators 'AND'. The first category was related to the descriptor 'challenges' OR problem* OR difficult* OR 'issues*'. The second category was related to antidepressant use which included: antidepressant* OR neuroleptic* OR 'depression pharmacotherapy*'. The third category was the population of interest: elderl* OR geriatri* OR older adult* OR 'older patients'. Any research conducted in a community, and/or a residential or institutionalised aged-care facility, and/or a hospital setting was taken into account.

Inclusion and exclusion criteria

Inclusion of articles which were as follows:

- Evaluated issues pertaining to diagnosis of depression and selecting pharmacotherapy for suitable older people.
- Reported on depressed individuals aged 65 or over or research which comprised of a sub-analysis of older people.
- Reported data from randomised or non-randomised trials.
- Written in English and published between January 2011 and August 2021.

Exclusion

- Non-English language publication.
- Review articles.
- Editorial papers.
- Only focused on non-pharmacological approach.

Reference lists of articles that were included were further searched manually for inclusion of further relevant articles. After removing the duplicates, the publications were screened for possible eligibility, at first from their titles and abstract and then the retrieved full texts.

Data extraction

Relevant data were reviewed from the included articles. Every study was evaluated by drafting a content description and a brief summary of the findings. Then, a narrative integration of the relevant evidence was reported. To ease the extraction, the data were entered into an Excel spreadsheet.

Key findings

The search strategy yielded 2500 articles. Of these, 1495 articles were excluded on the basis that they were irrelevant to the review based on their titles and abstracts. Of the remaining 1005 articles, 485 studies were review articles (either systematic or narrative review), 395 studies had participants below the age of 65 years, 42 studies did not imply antidepressant use, 28 articles were related to stigmatism and various treatment modalities, and 15 studies were not written in the English language. Six studies were duplicate publications. After a manual check of the reference lists of the included articles, 5 more articles were added, bringing the total number of studies to be included to 11.

The studies reported issues that need to be taken into consideration when identifying and managing elderly people with depression. The challenges associated with the difficulty in depression diagnosis (n = 11) prior to recommendation for a antidepressant were grouped into three groups: challenges associated with aging processes, challenges in recognising depressive symptoms, and challenges in distinguishing depression from cognitive impairment.

Challenges associated with ageing processes

Table 1 shows that two studies concluded that there were challenges associated with the ageing processes. Diniz *et al.* suggested ageing is a significant factor in the reduction of brain-derived neurotrophic factor (BDNF) levels. Altered BDNF levels in the older individuals have been linked to the onset of cognitive decline, depression and neurodegenerative disorders.[6] Disabato *et al.* described the onset of depressive symptoms as also influenced by ageing processes related to changes in cortical thickness, white matter hyperintensities and subcortical grey matter hyperintensities.[7]

Challenges in recognising depressive symptoms

Table 2 shows that five studies concluded that there were challenges in recognising depressive symptoms. Mulvahill *et al.* focused on the prevalence of the metabolic syndrome (MetS) that characterised as the coexistence of metabolic dysregulation and obesity in the depressed elderly was linked to increased recurrence of depression.[8] Turk *et al.* assessed patients with vascular depression who have substantially higher aggressive and auto-aggressive tendencies due to a reduced tolerance threshold.[9] Then, Sneed *et al.* and Feng *et al.* examined microbleeds scanned through magnetic resonance imaging (MRI) as being linked to late-onset depression (LOD) in older individuals.[10, 11]

Challenges in distinguishing depression from cognitive impairment

Table 2 shows that five studies concluded that there were challenges in distinguishing depression from cognitive impairment. Beheydt *et al.* addressed cognitive impairment as a part of depression in this elderly population.[12] Manifestation of the cognitive deficit is the

Table 1 Summary of the studies that concluded that there were challenges associated with the ageing processes

Issue	Author (year)	Design	Intervention	Outcome measures	Significant findings
Ageing process	Diniz *et al.* (2014)	A longitudinal double-blind, placebo-controlled trial study	Donepezil use on BDNF levels in depressed patients	Cognitive assessments and blood samples were taken to measure serum BDNF levels	Patients with LLD and MCI ($P = 0.004$) observed reduced BDNF levels throughout the 2-year follow-up. No effect of donepezil use on the BDNF. Ageing is a significant role in the decrease of BDNF levels
	Disabato *et al.* (2014)	A prospective, non-randomised, controlled trial study	12 weeks of sertraline treatment	The use of Montgomery–Asberg Depression Rating Scale (MADRS), neuropsychological testing and MRI scans	At 12th week, the LOD group was observed with a substantially smaller left anterior cingulate (Wilcoxon rank-sum test, $z¼ = 2.31$, $p¼ = 0.02$) but higher levels of WMHs and subcortical grey matter hyperintensities ($z¼ = 3.49$, $P < 0.01$ and $z¼ = 2.17$, $p¼ = 0.03$ accordingly)

same as other illnesses typically dementia and Alzheimer's disease. Yu *et al.*, Richard *et al.* and Chiu *et al.* investigated dementia to be substantially linked to depression in later life population.[13–15] Robinson *et al.* postulated the degenerative changes associated with Alzheimer's disease generate a parallel neurological core alongside depression.[16] All of these conditions make it difficult to be certain of a depression diagnosis in the geriatric patients.

Discussion

Papers from the year 2015 and later were included in this discussion section to correspond with the most recent evidence regarding challenges to prescribing antidepressants for the elderly.

Challenges associated with the difficulty in depression diagnosis

Depressed older patients frequently experience disability, functional decline, reduced quality of life and death from concomitant medical illnesses, changes that are assumed to be the normal parts of ageing processes.[7, 8] Clinicians are less likely to recognise that the elderly suffer from depression since they may present distinct symptoms from younger individuals, their prominent symptom is not sadness. They might also deny depression or grief but will complain about accompanying somatic symptoms, loss of focus and memory trouble.[9–12]

Physiological changes, especially association of depression with cognitive impairment, has the strongest evidence in which showing a focus on the presence of cognitive impairment alone results in depression in the elderly being underdiagnosed since there are other diseases correlated with cognitive deficits such as dementia and Alzheimer's disease. Even though the relation between depression and dementia is difficult to prove, the two illnesses typically appear to be connected.[13, 17] Among issues of physiological changes in older adults, cognitive impairment should be focused on, which is crucial for better screening and diagnosis establishment to differentiate the diseases for proper interventions and therefore better therapeutic outcomes.

The results determined that ruling out neurocognitive disorders is important to be integrated into the diagnosis of depression in later life. The cognitive symptoms should be closely evaluated first rather than being treated with antidepressants straightaway since depression in the older adults is frequently correlated to cognitive deficits, cognitive testing should always be included in regular evaluations of older individuals.

Recommendations

From the challenges highlighted in the review, several recommendations for best practice can be proposed. Determining the predictor variables of late-life depression might result in interventions that are better suited to the patients and can halt remission. Regular assessments of vascular risk, cognitive testing as well as attention to medication-related symptoms and shared decision-making regarding the management of older adults with depression are also vital components of the pharmacotherapy regimen plan.

Conclusion

Depression diagnoses and the decision to prescribe an antidepressant for the older population are complex. The study highlighted pertinent challenges to prescribers when older patients seek drug therapy for depression. This could have easily led to many depression cases gone

Table 2 Summary of the studies which concluded that there were challenges in recognising depressive symptoms and distinguishing depression from cognitive impairment

Issues	Author (year)	Design	Intervention	Outcome measures	Significant findings
Recognise depressive symptoms	Mulvahill *et al.* (2017)	A randomised controlled trial with open-label and protocolised study	Extended-release of venlafaxine for 12-week trial	Remission rate via MADRS of lower than 10 at last two visits	At 12 weeks, MetS was linked to a greater severity and chronicity of depression with venlafaxine at baseline and correlated to a longer duration to remission (remission hazard ratio = 0.71, 95% confidence interval [CI], 0.52 to 0.95)
	Turk *et al.* (2015)	A case-controlled clinical trial study	N/A	Questionnaires based on Rutherford and Fontaine criteria to assess depression, alexithymia, aggressiveness and personality functioning	Vascular disease in the vascular depression group with carotid stenosis (higher than 70%) or post-carotid stent operation was observed in 16% of patients. The matched non-VD group ($n¼ = 25$) showed no diagnosis of vascular disease
	Sneed *et al.* (2011)	A randomised clinical trial study	12-week trial of sertraline and nortriptyline	MRI scans for total hyperintensity, deep white matter hyperintensity (DWMH) and volume of periventricular hyperintensity (PVH). Remission via 24-item Hamilton Rating Scale for Depression score (HRDS) lower than 7 throughout 12 weeks	At 12 weeks, the patients were identified with a significant DWMH with7.14 times more likely than those with a low DWMH to not respond to antidepressant therapy ($P = 0.02$). PVH (odds ratio [OR] = 4.17, $P = 0.16$) and total volumes (OR = 5.00, $P = 0.05$) were affected equally
	Feng *et al.* (2014)	A clinical trial study	Patients were classified into early-onset depression (EOD), presenile onset depression (POD), LOD and control groups and scanned by MRI	15-item Geriatric Depression Scale (GDS) to assess depression severity. To find the independent risk variables for depression, logistic regression and linear regression were used	There was a greater GDS score (9.74 versus 7.82, $P = 0.001$) for patients with microbleeds in the LOD group. There is no change in GDS scores between the EOD and POD groups with and without microbleeds ($P > 0.05$)
Distinguishing depression from mild cognitive impairment	Beheydt *et al.* (2014)	A clinical trial study	Assess patients with recurrent MDD versus control group	Clinical depression tests, cognitive processing speed, memory tests and objective computerised fine motor skill assessments in a test battery	The patient group observed with a substantially longer reinspection time ($F = 3.89$, $P = 0.029$) with psychomotor performance impacted more by an increased cognitive load more than the control group
Distinguishing depression from dementia	Yu *et al.* (2020)	A nationwide, retrospective propensity score-matched cohort study	Patients were classified into the case and control groups associating dementia and depression	Relation of depression LOD and EOD with dementia based on sociodemographic characteristics	Dementia was substantially linked to depression (OR = 2.20, 95% CI, 1.53 to 3.14) particularly depressed female patients and older patients with depression having a higher risk of dementia than the control group (OR = 2.65, 95% CI, 1.78 to 3.93 and OR = 2.72, 95% CI, 1.41 to 5.24, accordingly)
	Richard *et al.* (2013)	A multiethnic community cohort study	Evaluated the association of depression with mild cognitive impairment (MCI) and dementia	10-item version of the Center for Epidemiological Studies Depression scale (CES-D) to assess depression severity, higher than 4 for MCI dementia	Depression was linked to prevalent cognitive deficit (OR = 1.4; 95% CI, 1.1 to 1.9) and dementia (2.2; 1.6 to 3.1), with likelihood of incident dementia (hazard ratio [HR] = 1.7; 95% CI, 1.2 to 2.3). Patients with cognitive deficit and coexisting depression at baseline had a greater potential to develop dementia (HR = 2.0; 95% CI, 1.2 to 3.4), particularly vascular dementia (4.3; 1.1 to 17.0)

Table 2 Continued

Issues	Author (year)	Design	Intervention	Outcome measures	Significant findings
	Chiu *et al.* (2017)	A clinical trial study	Alzheimer's disease versus dementia associated with depression	The severity of depression via HRDS, the Cornell Scale for Depression in Dementia and the depression subscale in Neuropsychiatric Inventory. The rates of depressive symptoms were compared between Alzheimer's disease and dementia	The frequency of major depression was greater ($P = 0.017$) in dementia (19.7%) than in Alzheimer's disease (8.7%). The severity of depression was higher in dementia than Alzheimer's disease according to HRDS ($P < 0.001$) and the Cornell Scale for Depression in Dementia ($P < 0.001$)
Distinguishing depression from Alzheimer's disease	Robinson *et al.* (2021)	A longitudinal study	Alzheimer's disease versus dementia associated with depression	Assessment using GDS and Alzheimer's disease (AD) onset determined by Braak stage, CERAD and Thal phase	There was a greater proportion of cognitively impaired individuals were present in the high severity pathology groups for the Thal phase ($P = 0.014$), CERAD score ($P < 0.001$) and Braak stage ($P < 0.001$). On the GDS30, those with cognitive impairment at passing showed greater than those with normal cognition ($P = 0.007$)

undiagnosed or misdiagnosed. The major findings were inconsistent, although there was compelling evidence. Further mixed-method research that is qualitative and quantitative research is required to investigate and outline areas for improvements.

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Author Contributions

All authors contributed equally to this work.

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Conflict of Interest

The authors declare no conflict of interest in the present work.

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